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Mary Hale, Information Branch Supervisor
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Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art* ***found****, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

  Types of relevant prior art found:
  - ☐ Foreign Patent(s)
  - ☐ Non-Patent Literature
    (journal articles, conference proceedings, new product announcements etc.)
- *Relevant prior art* ***not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC-Biotech-Chem Library, Remsen Bldg.

sira
Search and Information Resources Administration

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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: S. Kumar Examiner #: 69594 Date: 7/15/04
Art Unit: 1621 Phone Number 30 272-0610 Serial Number: 10/632,488
Mail Box and Bldg/Room Location: RFM 5D61 5C18 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. ME

****

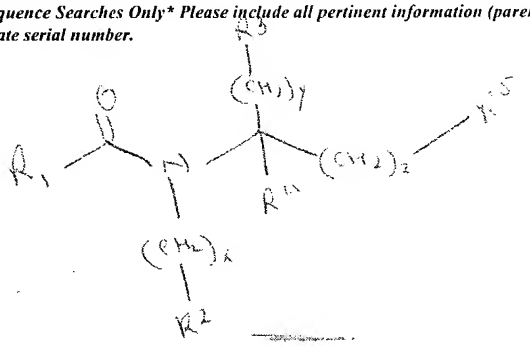
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

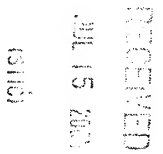
Title of Invention: Oxytocin inhibitors

Inventors (please provide full names): Andrew T. Nixon Robert Armour et al

Earliest Priority Filing Date: 8/08/02

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**





R^1 phenyl, aromatic heterocycle

R^2 phenyl, CPh, cycloalkyl(cyclic (aza with phenyl)), aromatic heterocycle R^6, $CONR^6R^6$ heterocycle

R^3 phenyl, het, R^6, cycloalkyl aromatic het.

R^4 H or CH_3

R^5 $CONH_2$, $CONHR^6$, $CONR^6R^6$, R^6, NH_2, $CH_2OCONHR^6$ etc.

R^6 alkyl

R^7 H, alkyl

R^8 alkyl or NR^7R^8

****

STAFF USE ONLY

Searcher: Noble Ifjan
Searcher Phone #:
Searcher Location:
Date Searcher Picked Up:
Date Completed: 7/25/04
Searcher Prep & Review Time: 60
Clerical Prep Time:
Online Time: 120

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#) 1
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN 98
Dialog
Questel/Orbit
Dr.Link (DUS)
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

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     (FILE 'HOME' ENTERED AT 07:49:07 ON 28 JUL 2004)

     FILE 'HCAPLUS' ENTERED AT 07:49:13 ON 28 JUL 2004
                E ARMOUR D/AU
L1           28 E3,E5,E16-18
                E BELL A/AU
L2          144 E3,E32-33
                E BELL ANDREW/AU
L3          100 E3,E13-14
                E EDWARS P/AU
                E EDWARDS P/AU
L4           98 E3,E11,E45-46
                E ELLIS D/AU
L5          196 E3,E45
                E HEPWORTH D/AU
L6           25 E3-6
                E LEWIS M/AU
L7          131 E3,E20,E83-84
                E SMITH C/AU
L8          422 E3
                E SMITH C R/AU
L9          160 E3-6
                E SMITH CHRISTPHER/AU
                E SMITH CHRISTOPHER/AU
L10         108 E3,E39-40
L11       10834 PFIZER/CS,PA
L12           2 L1-10 AND OXYTOCIN
L13           7 L11 AND OXYTOCIN
L14           6 L13 NOT L12

     FILE 'REGISTRY' ENTERED AT 08:08:19 ON 28 JUL 2004

     FILE 'HCAPLUS' ENTERED AT 08:08:23 ON 28 JUL 2004
L15             TRA L12 1- RN :      313 TERMS

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L16          313 SEA L15

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L17             TRA L14 1- RN :      212 TERMS

     FILE 'REGISTRY' ENTERED AT 08:08:29 ON 28 JUL 2004
L18          212 SEA L17
L19          523 L16 OR L18

=> b hcap
FILE 'HCAPLUS' ENTERED AT 08:07:47 ON 28 JUL 2004
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FILE COVERS 1907 - 28 Jul 2004 VOL 141 ISS 5
FILE LAST UPDATED: 27 Jul 2004 (20040727/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d all l12 tot

L12 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:203814 HCAPLUS
DN 140:253449
ED Entered STN: 14 Mar 2004
TI Preparation of heterocyclylcarboxamides as **oxytocin** inhibitors
IN **Armour, Duncan Robert; Bell, Andrew Simon; Edwards, Paul John; Ellis, David; Hepworth, David; Lewis, Mark Llewellyn; Smith, Christopher Ronald**
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D213-82
ICS C07D319-18; C07D213-81; C07D405-12; C07D521-00; C07D401-12; C07C255-57; A61K031-44; A61K031-4427; A61P015-04; A61P015-10
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 28, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004020414	A1	20040311	WO 2003-IB3705	20030813

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2002-19961 A 20020828
OS MARPAT 140:253449
AB R1CON[(CH2)xR2]C(R4)[(CH2)yR3](CH2)zR5 [R1 = (substituted) Ph, heteroaryl; R2 = (substituted) Ph, OPh, cycloalkyl, heteroaryl, heterocyclyl, etc.; R3 = (substituted) (fused) Ph, heterocyclyl, heteroaryl, R6, etc.; R4 = H, Me; R5 = CONH2, NH2, OH, R6, NHR6, OR6, CONHR6, (substituted) heteroaryl, etc.; R6 = alkyl; x, y, z = 0-2], were prepared Thus, 4-chlorobenzylamine, o-tolualdehyde, 2-aminonicotinic acid, and (4-isocyanocyclohex-3-enyl)benzene (preparation given) were stirred in MeOH/cyclohexane to give a residue which was stirred in aqueous HCl/THF to give 2-amino-N-[2-amino-1-(2-methylphenyl)-2-oxoethyl]-N-(4-chlorobenzyl)nicotinamide. Title compds. at 10 .mu.M gave >70% inhibition of oxytocin.

ST heterocyclylcarboxamide prepn **oxytocin** inhibitor; neuropsychiatric obsessive compulsive disorder treatment heterocyclylcarboxamide prepn; ocular arterial nephrotic hypertension treatment heterocyclylcarboxamide prepn; liver cirrhosis congestive heart failure treatment heterocyclylcarboxamide prepn; dysmenorrhea premature birth benign prostatic hypertrophy treatment heterocyclylcarboxamide prepn; obesity feeding eating appetite disorder treatment heterocyclylcarboxamide prepn; labor complication preterm labor premature ejaculation treatment heterocyclylcarboxamide prepn; sexual dysfunction treatment heterocyclylcarboxamide prepn

IT Addition reaction
(Ugi; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT Prostate gland, disease
(benign hyperplasia, treatment; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT Parturition
(complications, treatment; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT Appetite
Sexual behavior
(disorder, treatment; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT Heart, disease
(failure, treatment; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT Hypertension
(nephrotic hypertension treatment; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT Mental disorder
(obsession-compulsion, treatment; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT Sexual behavior
(premature ejaculation, treatment; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT Parturition
(premature, treatment; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT Antihypertensives
Antiobesity agents
Drug delivery systems
Human
(preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT Cirrhosis
Dysmenorrhea
Glaucoma (disease)
Hypertension
Mental disorder
Obesity
(treatment; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT 669084-63-3P, 2-Amino-N-[2-amino-1-(2-methylphenyl)-2-oxoethyl]-N-(4-chlorobenzyl)nicotinamide 669084-64-4P, N-[2-Amino-1-(3-methoxyphenyl)-2-oxoethyl]-4-cyano-N-(4-methylbenzyl)benzamide 669084-65-5P, N-[3-Amino-1-(3-methoxyphenyl)-3-oxopropyl]-4-methyl-N-(4-methylbenzyl)nicotinamide 669084-66-6P, 2-Amino-N-[(1S)-3-amino-3-oxo-1-phenylpropyl]-N-(4-methylbenzyl)nicotinamide 669084-67-7P, 5-Chloro-2-methylthio-N-[2-amino-1-[1,4-benzodioxan-6-yl]-2-oxoethyl]-N-(4-methylbenzyl)pyrimidine-4-carboxamide 669084-68-8P, 5-Chloro-2-amino-N-[2-amino-1-[1,4-benzodioxan-6-yl]-2-oxoethyl]-N-(4-methylbenzyl)pyrimidine-

4-carboxamide 669084-69-9P, 2-Amino-N-[carbamoyl-(2,3-dihydro-benzo[1,4]dioxin-6-yl)methyl]-4,6-dimethyl-N-(4-methylbenzyl)nicotinamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT 50-56-6, **Oxytocin**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT

669084-70-2P	669084-72-4P	669084-74-6P	669084-76-8P	669084-77-9P
669084-79-1P	669084-80-4P	669084-81-5P	669084-82-6P	669084-83-7P
669084-84-8P	669084-85-9P	669084-86-0P	669084-87-1P	669084-88-2P
669084-89-3P	669084-90-6P	669084-91-7P	669084-92-8P	669084-93-9P
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669086-99-1P	669087-00-7P	669087-01-8P	669087-02-9P	669087-03-0P
669087-04-1P	669087-05-2P	669087-06-3P	669087-07-4P	669087-08-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT 669087-09-6P 669087-10-9P 669087-11-0P 669087-12-1P 669087-13-2P
669087-14-3P 669087-15-4P 669087-16-5P 669087-17-6P 669087-18-7P
669087-19-8P 669087-20-1P 669087-21-2P 669087-22-3P 669087-23-4P
669087-24-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT 74-89-5, Methylamine, reactions 75-04-7, Ethylamine, reactions
100-46-9, Benzylamine, reactions 104-84-7, 4-Methylbenzylamine
104-86-9, 4-Chlorobenzylamine 104-87-0, p-Tolualdehyde 123-00-2,
3-(4-Morpholinyl)-1-propylamine 124-40-3, Dimethylamine, reactions
529-20-4, o-Tolualdehyde 557-66-4, Ethylamine hydrochloride 591-31-1,
m-Anisaldehyde 593-51-1, Methylamine hydrochloride 619-65-8,
4-Cyanobenzoic acid 934-60-1, 6-Methylpyridine-2-carboxylic acid
2260-00-6 2942-59-8, 2-Chloronicotinic acid 3222-50-2,
4-Methylnicotinic acid 3952-66-7, Methyl 2-ketobutyrate 4637-24-5, Dmf
dimethyl acetal 5345-47-1, 2-Aminonicotinic acid 25016-11-9,
1-Methyl-1H-pyrazole-4-carboxaldehyde 29668-44-8, Benzodioxane-6-carboxaldehyde 41110-28-5, 3-Methylpyrazine-2-carboxylic acid
61727-33-1, 5-Chloro-2-(methylsulfanyl)pyrimidine-4-carboxylic acid
68208-19-5 69950-65-8 79686-03-6, Methyl 5-chloro-2-methylthiopyrimidine-4-carboxylate 101395-71-5, 2-(1H-Pyrazol-1-yl)ethylamine 103365-47-5 106837-89-2, 2-Amino-4,6-dimethylnicotinic acid 120351-90-8, 2-(2-Fluorophenoxy)ethylamine 128798-29-8
155790-12-8, 6-Methyl-2-methylaminonicotinic acid 158063-66-2,
4-Trifluoromethylnicotinic acid 179897-89-3, 5-Bromo-2-fluorobenzonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

IT 32399-13-6P, 2-Methylaminonicotinic acid 33522-80-4P,
2-Benzylaminonicotinic acid 67751-16-0P 128798-39-0P 218301-22-5P,
2-Fluoro-5-formylbenzonitrile 669087-25-6P, 2-Ethylaminonicotinic acid
669087-26-7P 669087-27-8P, Methyl 3-amino-3-(3-methoxyphenyl)propanoate
669087-28-9P 669087-29-0P 669087-30-3P 669087-31-4P 669087-32-5P
669087-33-6P 669087-34-7P 669087-35-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclylcarboxamides as **oxytocin** inhibitors)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Adipogenix Inc; WO 03007888 A 2003 HCAPLUS
(2) Anon; ComGenex Product List 2003
(3) Anon; TimTec Overseas Stock 2003
(4) Aries, R; FR 2161776 A 1973 HCAPLUS
(5) Bragg, R; TETRAHEDRON LETTERS 2002, V43(11), P1955 HCAPLUS
(6) David, S; BULLETIN DE LA SOCIETE CHIMIQUE DE FRANCE 1965, 8, P2301 HCAPLUS
(7) Dunina, V; ZHURNAL ORGANICHESKOI KHIMII 1977, V13(8), P1616 HCAPLUS
(8) Francis, G; WO 03037274 A 2003 HCAPLUS
(9) Hans, G; US 2496882 A 1950 HCAPLUS
(10) Potapov, V; ZHURNAL OBSHCHEI KHIMII 1962, V32, P1187 HCAPLUS
(11) Procter & Gamble; WO 9906340 A 1999 HCAPLUS
(12) Sasaki, Y; CHEMICAL & PHARMACEUTICAL BULLETIN 1993, V41(3), P415 HCAPLUS
(13) Tokuyama Soda Kk; EP 0189774 A 1986 HCAPLUS
(14) Tomita, K; US 4060402 A 1977 HCAPLUS
(15) Wyeth; WO 0244142 A 2002 HCAPLUS

L12 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:317274 HCAPLUS
DN 126:341849
ED Entered STN: 17 May 1997
TI **Oxytocin** - a possible growth promotion factor for GH3 cell line
AU Catrina, S. B.; **Lewis, M.**; Caragheorgheopol, Andra; Cucu, C.; Coculescu, M.; Scanlon, M.
CS "Carol Davila" University of Medicine and Pharmacy, Bucharest, Rom.
SO Romanian Journal of Endocrinology (1995), 33(1-4), 57-62
CODEN: RJENE9; ISSN: 1221-356X
PB Editura Academiei Romane
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB There is not a general agreement about the hypothalamic factors involved in the pathogenesis of pituitary tumors. This study shows the influence of oxytocin on the proliferation rate of the rat somatomamotroph GH3-cell line. GH3 cells were maintained in Ham's F-10 supplemented with 15% horse serum, 2.5% fetal calf serum and antibiotics (100 .mu.g/mL streptomycin, 100 U/mL penicillin, amphotericin B). Cells were subcultured by trypsinization (0.5 mg/mL in Ca2+ and Mg2+ free Earle's balanced salts solution). The dose/response curve was calculated between 10-6 - 10-6 mol of oxytocin (OXT), arginine vasopressin (AVP), arginine vasotocin (AVT), and the specific oxytocin receptor agonist T4-G7-oxytocin (TGOT). The proliferation rate was evaluated by H3-incorporation and XTT cell proliferation assay. All results were assayed in quadruplicate and the proliferation rate expressed as a percentage of control values. OXT and TGOT produced a dose dependent increase in the proliferation rate. The maximum affect of TGOT (200% for H3-thymidine incorporation and 6% for XTT) is greater than for OXT (150% at H3-thymidine incorporation). AVT inhibits the proliferation rate in a dose dependent manner (maximum decrease 60% for H3-thymidine incorporation). AVP does not show significant effects. The greater effect of the agonist TGOT compared to OXT can be explained by the fact that OXT can act on other nonapeptide receptors. It is also possible that OXT and TGOT have different intracellular messengers on cellular proliferation. In conclusion OXT and its specific agonist (TGOT) enhance the proliferation of the rat pituitary GH3 cell line. Although the effect is small, it is dose dependent at physiol. concns. suggesting that OXT could be a growth promoting factor in somatomamotroph tumors.
ST **oxytocin** growth promotion factor GH3 cell; somatomamotroph tumor growth promoter **oxytocin**
IT Animal cell line
(GH3; **oxytocin** as possible growth promotion factor for GH3 cell line)
IT Pituitary gland
(neoplasm; **oxytocin** as possible growth promotion factor for GH3 cell line)
IT Cell proliferation
(**oxytocin** as possible growth promotion factor for GH3 cell line)
IT **Oxytocin** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**oxytocin** as possible growth promotion factor for GH3 cell line)
IT 50-56-6, **Oxytocin**, biological studies 60786-59-6, Thr4-Gly7-**Oxytocin**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL

(Biological study)
(**oxytocin** as possible growth promotion factor for GH3 cell line)

IT 113-79-1, Arginine vasopressin 113-80-4, Arginine vasotocin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**oxytocin** as possible growth promotion factor for GH3 cell line)

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L14 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:871580 HCAPLUS
DN 140:71495
ED Entered STN: 07 Nov 2003
TI MrgX2 is a High Potency Cortistatin Receptor Expressed in Dorsal Root Ganglion
AU Robas, Nicola; Mead, Emma; Fidock, Mark
CS Department of Target Genomics, **Pfizer** Global Research and Development, Kent, CT13 N9J, UK
SO Journal of Biological Chemistry (2003), 278(45), 44400-44404
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 13
AB MrgX2 is a recently identified orphan G-protein-coupled receptor whose ligand and physiol. function were unknown. Here we describe cortistatin, a neuropeptide for which no specific receptor has been identified previously, as a high potency ligand at MrgX2. Cortistatin has several biol. functions including roles in sleep regulation, locomotor activity, and cortical function. Using a "reverse pharmacol." approach, we have identified a number of addnl. cyclic peptide agonists for MrgX2, determined their rank order of potency, and demonstrated that this receptor has a pharmacol. profile distinct from the other characterized members of the Mrg (Mas-related genes) family. In MrgX2-expressing cells, cortistatin-stimulated increases in intracellular Ca2+ but had no effect on basal or forskolin-stimulated cAMP levels, suggesting that this receptor is Gq-coupled. Immunohistochem. and quant. PCR studies show MrgX2 to have a limited expression profile, both peripheral and within the central nervous system, with highest levels in dorsal root ganglion.
ST MrgX2 cortistatin receptor agonist dorsal root ganglion calcium
IT G proteins (guanine nucleotide-binding proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Gq; MrgX2, a Ca++-dependent Gq-protein-coupled receptor, is a high potency cortistatin receptor expressed in dorsal root ganglion and other tissues)
IT Human
Intestine
Testis
(MrgX2, a Ca++-dependent Gq-protein-coupled receptor, is a high potency cortistatin receptor expressed in dorsal root ganglion and other tissues)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MrgX2; MrgX2, a Ca++-dependent Gq-protein-coupled receptor, is a high potency cortistatin receptor expressed in dorsal root ganglion and other tissues)

IT Ganglion
(spinal; MrgX2, a Ca++-dependent Gq-protein-coupled receptor, is a high potency cortistatin receptor expressed in dorsal root ganglion and other tissues)
IT 50-56-6, **Oxytocin**, biological studies 73-24-5, Adenine, biological studies 113-79-1, Arginine vasopressin 550-21-0, Isotocin 33507-63-0, Substance P 51110-01-1, Somatostatin 14 54518-51-3, 3-14-Somatostatin (sheep) 58976-46-8, D-Trp8-somatostatin 60498-04-6 75037-27-3, Somatostatin 28 76622-26-9, 1-22-Peptide E (cattle adrenal medulla) 83150-76-9, Octreotide 84211-54-1 88161-22-2, Dynorphin A 99566-27-5, Neuropeptide FF (cattle) 140703-51-1, Hexarelin 170713-75-4, NOCICEPTIN 192387-38-5 192387-39-6 207678-81-7, HS014 212370-59-7, HS024 311309-27-0 331627-76-0, Somatostatin 7-14 331627-82-8 331627-85-1 412961-36-5 412961-39-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MrgX2 agonist; MrgX2, a Ca++-dependent Gq-protein-coupled receptor, is a high potency cortistatin receptor expressed in dorsal root ganglion and other tissues)
IT 189450-19-9
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(MrgX2 agonist; MrgX2, a Ca++-dependent Gq-protein-coupled receptor, is a high potency cortistatin receptor expressed in dorsal root ganglion and other tissues)
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MrgX2, a Ca++-dependent Gq-protein-coupled receptor, is a high potency cortistatin receptor expressed in dorsal root ganglion and other tissues)
IT 186901-48-4, Cortistatin-14
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(MrgX2, a Ca++-dependent Gq-protein-coupled receptor, is a high potency cortistatin receptor expressed in dorsal root ganglion and other tissues)
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(18) Siehler, S; Naunyn-Schmiedeberg's Arch Pharmacol 1999, V360, P510 HCAPLUS
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L14 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:610431 HCAPLUS
DN 139:144014
ED Entered STN: 08 Aug 2003
TI Treatment of male sexual dysfunction with compositions containing a selective **oxytocin** antagonist
IN Naylor, Alasdair Mark; Russell, Rachel Jane; Street, Stephen Derek Albert; Tang, Kim-Wah; Van der Graaf, Pieter Hadewijn; Wayman, Christopher Peter
PA **Pfizer** Limited, UK; **Pfizer** Inc.
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D295-26
ICS A61K031-495; A61P015-00; A61K045-06
CC 1-12 (Pharmacology)
Section cross-reference(s): 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003064402	A1	20030807	WO 2003-IB140	20030120
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003229001	A1	20031211	US 2003-350924	20030124
PRAI	GB 2002-2282	A	20020131		
	US 2002-357445P	P	20020214		
	US 2002-357445P	P	20020214		

AB A composition comprising a selective oxytocin antagonist for use in the treatment and/or prevention of a male ejaculatory disorder; which selective oxytocin antagonist is optionally admixed with a pharmaceutically acceptable carrier, diluent or excipient.
ST male sexual dysfunction treatment **oxytocin** antagonist
IT 5-HT agonists
(5-HT1B, as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)
IT 5-HT agonists
(5-HT1D, as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)
IT 5-HT agonists
(5-HT2C, as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)
IT 5-HT antagonists
(5-HT3, as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)
IT Rauvolfia
(Rauwolfia alkaloids as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)
IT Alkaloids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Rauwolfia alkaloids as auxiliary treatment agents; treatment of male

sexual dysfunction with compns. containing an **oxytocin** antagonist)

IT 5-HT agonists
5-HT antagonists
5-HT reuptake inhibitors
Antidepressants
(as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)

IT Sexual behavior
(disorder; treatment of male sexual dysfunction with compns. containing a selective **oxytocin** antagonist)

IT Drug screening
(of compds. that can prevent/treat a male ejaculatory disorder; treatment of male sexual dysfunction with compns. containing a selective **oxytocin** antagonist)

IT Sexual behavior
(premature ejaculation; treatment of male sexual dysfunction with compns. containing a selective **oxytocin** antagonist)

IT **Oxytocin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of male sexual dysfunction with compns. containing a selective **oxytocin** antagonist)

IT Drug delivery systems
Drug targets
(treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)

IT Antidepressants
(tricyclic, as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)

IT Adrenoceptor antagonists
(.alpha.-, as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)

IT Adrenoceptor antagonists
(.alpha.1-, as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)

IT Adrenoceptor antagonists
(.alpha.2-, as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline 50-49-7, Imipramine 50-60-2, Phentolamine 51-50-3, Dibenamine 59-96-1, Phenoxybenzamine 59-98-3, Tolazoline 65-28-1, Phentolamine mesylate 72-69-5, Nortriptyline 146-48-5, Yohimbine 303-49-1, Clomipramine 438-60-8, Protriptyline 739-71-9, Trimipramine 1668-19-5, Doxepine 4205-90-7, Clonidine 10262-69-8, Maprotiline 14028-44-5, Amoxapine 19216-56-9, Prazosin 19794-93-5, Trazodone 26844-12-2, Indoramin 34911-55-2, Bupropion 35795-16-5, Trimazosin 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 57149-07-2, Naftopidil 57368-81-7, SNAP 1069 59729-33-8, Citalopram 61869-08-7, Paroxetine 63590-64-7, Terazosin 72822-12-9, Dapiprazole 74191-85-8, Doxazosin 79617-96-2, Sertraline 79944-58-4, Idazoxan 81403-80-7, Alfuzosin 83366-66-9, Nefazodone 85650-52-8, Mirtazapine 89197-32-0, Efaroxan 89565-68-4, Tropisetron 90402-40-7, Abanoquil 93413-69-5, Venlafaxine 99614-02-5, Ondansetron 102670-46-2, Batanopride 106133-20-4, Tamsulosin 109889-09-0, Granisetron 115956-13-3, MDL-73147EF 146714-97-8, WAY-100635 152735-23-4, Recordati 15/2739 157066-76-7, SNAP 5089 169505-93-5, RS17053 194674-19-6, SL 89.0591 208516-87-4, NAD-299
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)

IT 9001-66-5, Monoamine oxidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors as adjuvant treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)
IT 9025-82-5, Phosphodiesterase 9068-52-4, Phosphodiesterase 5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors as auxiliary treatment agents; treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)
IT 50-56-6, **Oxytocin**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of male sexual dysfunction with compns. containing a selective **oxytocin** antagonist)
IT 148927-60-0, L368899
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of male sexual dysfunction with compns. containing an **oxytocin** antagonist)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Hadewijn, G; WO 0203995 A 2002 HCAPLUS
(2) Merck & Co Inc; EP 0614894 A 1994 HCAPLUS
(3) Naylor, A; BJU BRITISH JOURNAL OF UROLOGY 1998, V81(3), P424 HCAPLUS
(4) Veber, D; WO 9414438 A 1994 HCAPLUS
(5) Williams, P; JOURNAL OF MEDICINAL CHEMISTRY 1994, V37, P565 HCAPLUS

L14 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:465801 HCAPLUS
DN 137:52344
ED Entered STN: 21 Jun 2002
TI Treatment of male sexual dysfunction
IN Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn; Wayman, Christopher Peter
PA **Pfizer** Limited, UK; **Pfizer** Inc.
SO PCT Int. Appl., 179 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
ICS A61P015-10
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 2
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002047670	A1	20020620	WO 2001-IB2399	20011210
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002028799	A1	20020307	US 2001-895367	20010629
	US 2002102707	A1	20020801	US 2001-905846	20010713
	AU 2002020977	A5	20020624	AU 2002-20977	20011210
	EP 1347750	A1	20031001	EP 2001-270206	20011210
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRAI GB 2000-30647 A 20001215
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GB 2001-9910 A 20010423
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US 2001-895367 A 20010629
US 2001-905846 A 20010713
GB 2001-20679 A 20010824
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GB 2000-17387 A 20000714
US 2000-219100P P 20000718
US 2000-220908P P 20000726
US 2001-265358P P 20010131
GB 2001-6167 A 20010313
GB 2001-8483 A 20010404
WO 2001-IB2399 W 20011210

AB The use of an inhibitor of a neuropeptide Y (NPY), preferably of a NPY Y1 receptor, which inhibitor is selective for an NPY or NPY Y1 receptor associated with male genitalia, in the preparation/manufacture of a medicament for the treatment or prevention of male erectile dysfunction (MED).

ST male sexual dysfunction neuropeptide Y inhibitor sequence

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5HT6, modulators; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT Dopamine agonists
(D2; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT Dopamine agonists
(D3; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ORL1 (opioid receptor-like 1), agonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT Neuropeptide Y receptors
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Y1; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT Bombesin receptors
Endothelin receptors
Gastrin-releasing peptide receptors
Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antiestrogens; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT Appetite
(bulimia; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT Ion channel blockers
(calcium; neuropeptide Y inhibitors for treatment of male sexual

dysfunction)
IT Drug delivery systems
(carriers; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Penis
(corpus cavernosum; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Appetite
(disorder; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Alkaloids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ergot; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Prostaglandins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Sexual behavior
(impotence; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(intermediate conductance calcium-activated, modulators; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Reproductive organ
(male; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor, agonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators of, for noradrenaline, dopamine, and serotonin; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Cannabinoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT 5-HT agonists
5-HT antagonists
Anesthesia
Anorexia
Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Antiobesity agents
Blood pressure
Dopamine agonists
Fluorometry
Human
Nervous system agents
Obesity
Opioid antagonists
Platelet aggregation inhibitors
Protein sequences
Purinoceptor agonists
Vasodilators
cDNA sequences

(neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Estrogens
Opioids
Prostaglandins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Anti-inflammatory agents
(nonsteroidal; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Drug delivery systems
(oral; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Nerve
(pelvic; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Sexual behavior
(penile erection; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Ion channel openers
(potassium; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Anti-inflammatory agents
(steroidal; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-HT1A, modulators; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-HT2A, modulators; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-HT3, modulators; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Bombesin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB1, antagonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Bombesin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB2, antagonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Bombesin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB3, antagonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT Adrenoceptor antagonists
(.alpha.-; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT 72162-96-0, Thromboplastin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-activating factor inhibitors; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-sensitizing agents; neuropeptide Y inhibitors for treatment of male sexual dysfunction)
IT 9036-21-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(III, inhibitors; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT 50-56-6, **Oxytocin**, biological studies 57576-52-0, Thromboxane a2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT 138238-81-0, Endothelin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT 9028-35-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors, statins; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT 9000-81-1, Acetylcholinesterase 9002-04-4, Thrombin 9025-82-5, Phosphodiesterase 9068-52-4, Phosphodiesterase v 9068-54-6, Phosphodiesterase ii 82785-45-3, Neuropeptide Y
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT 9015-82-1, Angiotensin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT 58-00-4, Apomorphine 58-18-4, Methyl testosterone 58-22-0, Tostrelle 59-92-7, L Dopa, biological studies 63-05-8D, Androstenedione, derivs. 74-79-3, L Arginine, biological studies 81-81-2, Warfarin 520-85-4, Medroxyprogesterone 521-18-6, Dihydrotestosterone 8001-27-2, Hirudin 9005-49-6, Heparin, biological studies 9039-53-6, Urokinase plasminogen activator 28860-95-9, Carbidopa 29094-61-9, Glipizide 37221-79-7, Vasoactive intestinal peptide 82707-54-8, Neutral endopeptidase 85637-73-6, Atrial natriuretic factor 88150-42-9, Amlodipine 97322-87-7, Rezulin 114471-18-0, Atrial natriuretic peptide b 114798-26-4, Losartan 120014-06-4, Donepezil 127830-04-0, Atrial natriuretic peptide c 128908-32-7, Melanocortin 134523-00-5, Atorvastatin 139639-23-9, Tissue plasminogen activator
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transporters for; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT 438443-44-8, 2: PN: WO0247670 SEQID: 1 unclaimed DNA 438443-45-9, 3: PN: WO0247670 SEQID: 2 unclaimed DNA 438443-46-0, 4: PN: WO0247670 SEQID: 3 unclaimed DNA 438443-47-1, 5: PN: WO0247670 SEQID: 4 unclaimed DNA 438443-48-2, 6: PN: WO0247670 SEQID: 5 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; treatment of male sexual dysfunction)

IT 438443-49-3
RL: PRP (Properties)
(unclaimed protein sequence; treatment of male sexual dysfunction)

IT 438190-17-1
RL: PRP (Properties)
(unclaimed sequence; treatment of male sexual dysfunction)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Erwin, F; WO 9852890 A 1998 HCAPLUS
(2) Naylor, A; BRITISH JOURNAL OF UROLOGY 1998, V81(3), P424 HCAPLUS
(3) Pfizer Ltd; EP 1097718 A 2001 HCAPLUS
(4) Pollard, P; WO 0170708 A 2001 HCAPLUS
(5) Squibb Bristol Myers Co; WO 0185098 A 2001 HCAPLUS
(6) Squibb Bristol Myers Co; WO 0185173 A 2001 HCAPLUS
(7) Squibb Bristol Myers Co; WO 0185690 A 2001 HCAPLUS

L14 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:51273 HCAPLUS
DN 136:96099
ED Entered STN: 18 Jan 2002
TI Treatment of male sexual dysfunction
IN Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn; Wayman, Christopher Peter
PA **Pfizer** Limited, UK; **Pfizer** Inc
SO PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-55
ICS A61K031-401; A61K031-4166; A61K031-41; A61K031-421; A61K031-4365; A61K031-17; A61K031-16
CC 1-12 (Pharmacology)
Section cross-reference(s): 24, 25, 27, 28
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002003995	A2	20020117	WO 2001-IB1187	20010702
	WO 2002003995	A3	20020418		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002052370	A1	20020502	US 2001-893585	20010628
	EP 1296687	A2	20030402	EP 2001-947709	20010702
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004502735	T2	20040129	JP 2002-508449	20010702
	ZA 2003000121	A	20040121	ZA 2003-121	20030106
	ZA 2003000120	A	20040126	ZA 2003-120	20030106
PRAI	GB 2000-16684	A	20000706		
	GB 2000-30647	A	20001215		
	GB 2001-6167	A	20010313		
	GB 2001-8483	A	20010404		
	US 2000-219100P	P	20000718		
	GB 2001-1584	A	20010122		
	US 2001-274957P	P	20010312		
	WO 2001-IB1187	W	20010702		

OS MARPAT 136:96099
AB The present invention relates to the use of neutral endopeptidase inhibitors (NEPi) and a combination of NEPi and phosphodiesterase type (PDE5) inhibitor for the treatment of male sexual dysfunction, in

particular MED.

ST male sexual dysfunction neutral endopeptidase inhibitor

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ORL1 (opioid receptor-like 1), modulators; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Neuropeptide Y receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Y5, antagonists; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Neuropeptide Y receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Y1, antagonists; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT VIP receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Endothelin receptors
Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antiestrogens; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Ion channel blockers
(calcium; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Sexual behavior
(disorder, male; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dopamine-transporting, modulators; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Sexual behavior
(ejaculation, disorder; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Alkaloids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ergot; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Anticholesteremic agents
(fibrates and statins; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Sexual behavior
(impotence; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor, agonists; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Cannabinoid receptors
Estrogen receptors
Opioid receptors
Oxytocin receptors
Vasopressin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(norepinephrine transporter, modulators; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Drug delivery systems
(oral; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Ion channel openers
(potassium; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Sexual behavior
(premature ejaculation; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serotonin transporter, modulators; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Drug delivery systems
(tablets; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 5-HT agonists
5-HT antagonists
Angiotensin receptor antagonists
Anticoagulants
Dopamine agonists
Drug interactions
Drug screening
Opioid antagonists
Platelet aggregation inhibitors
Purinoceptor agonists
Vasodilators
(treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Estrogens
Opioids
Prostaglandins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Adrenoceptor antagonists
(.alpha.-; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 57576-52-0, Thromboxane A2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 82785-45-3, Neuropeptide Y
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors and agonists; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 128908-32-7, Melanocortin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancers; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9028-35-7, HMG-CoA reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors, statins; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9000-81-1, Acetylcholinesterase 9040-59-9, Phosphodiesterase II 9068-52-4, Phosphodiesterase V 82707-54-8, Neutral endopeptidase 138238-81-0, Endothelin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9036-21-9, Phosphodiesterase 8
RL: BSU (Biological study, unclassified); BIOL (Biological study) (isoforms, inhibitors; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9088-07-7, Natriuretic factor 85637-73-6, Atrial natriuretic factor
RL: BSU (Biological study, unclassified); BIOL (Biological study) (modulators; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (sensitizing agents; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 125978-95-2, Nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (substrates; treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 9015-82-1, Angiotensin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study) (treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 337962-68-2P 337962-69-3P 337962-70-6P 337962-71-7P 337962-72-8P 337962-73-9P 337962-74-0P 388630-36-2P 388630-55-5P
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 58-22-0, Testosterone 71-58-9, Medroxyprogesterone acetate 520-85-4, Medroxyprogesterone 521-18-6, Dihydrotestosterone 37221-79-7, Vasoactive intestinal peptide 37221-79-7D, Vasoactive intestinal peptide, analogs 139755-83-2, Sildenafil 147676-53-7 171596-29-5, IC-351 215297-27-1 224785-90-4, Vardenafil 334826-98-1 334827-47-3 334827-59-7 335077-64-0 335077-70-8 389128-36-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of male sexual dysfunction using neutral endopeptidase

inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 98-10-2, Benzenesulfonamide 108-33-8, 2-Amino-5-methyl-1,3,4-thiadiazole 7663-77-6, N-(3-Aminopropyl)-2-pyrrolidinone 14068-53-2, 2-Amino-5-ethyl-1,3,4-thiadiazole 59892-44-3 118755-30-9 118755-86-5 118756-03-9 118783-85-0 118786-35-9 136834-71-4 136834-85-0 136850-24-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 337962-78-4P 337962-79-5P 337962-80-8P 337962-81-9P 337962-83-1P 337962-84-2P 337962-91-1P 337962-93-3P 388630-52-2P 388630-83-9P 388631-26-3P 388631-29-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT 388630-37-3P 388630-54-4P 389083-04-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

L14 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:480269 HCAPLUS
DN 119:80269
ED Entered STN: 21 Aug 1993
TI Natural proteins or hydrolyzates in pharmaceutical compositions to protect bioactive peptides from enzymic inactivation
IN Amidon, Gordon L.; Leesman, Glen D.; Sinko, Patrick J.
PA **Pfizer** Inc., USA
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-42
ICA C07K015-10
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9311799	A1	19930624	WO 1992-US9336	19921109
	W: AU, CA, FI, HU, JP, KR, NO, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
	AU 9230583	A1	19930719	AU 1992-30583	19921109
	EP 617626	A1	19941005	EP 1992-924173	19921109
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
	JP 06510796	T2	19941201	JP 1992-510892	19921109
	HU 69785	A2	19950928	HU 1994-1824	19921109
	ZA 9209761	A	19940617	ZA 1992-9761	19921217
	FI 9402938	A	19940617	FI 1994-2938	19940617
	NO 9402323	A	19940617	NO 1994-2323	19940617
	US 6153592	A	20001128	US 1994-244715	19940908
PRAI	US 1991-810593	A1	19911218		

WO 1992-US9336 A 19921109

AB Proteins or peptides, which may be prepared form natural sources, enhance the bioavailability of proteolytically-labile therapeutic agents which, in the absence of the protein or peptide would suffer enzymic inactivation upon administration. Soy flour was hydrolyzed and proteins were ultrafiltered and fractions with mol. weight .ltoreq.30kDa were separated and freeze-dried. Terlakiren (I) 200 mg, was coadministered with 1g of above protein fractions in 150mL water to dogs and the serum level of I was measured. The AUC of I was 0.286 as compared to 0.049 .mu.g/h/mL for controls.

ST enzyme protection protein peptide; soy protein terlakiren bioavailability enhancement

IT Enkephalins
Immunoglobulins
Interferons
RL: PROC (Process)
(enzymic protection of, in pharmaceuticals, with peptides and proteins)

IT Gonadotropins
RL: PROC (Process)
(enzymic protection of, in pharmaceuticals, with proteins and peptides)

IT Caseins, biological studies
Peptides, biological studies
Protein hydrolyzates
Proteins, biological studies
RL: BIOL (Biological study)
(for prevention of enzymic inactivation of pharmaceuticals)

IT Glutens
RL: BIOL (Biological study)
(from wheat, proteins and peptides from, for prevention of enzymic inactivation of pharmaceuticals)

IT Pharmaceutical dosage forms
(natural proteins and peptides in, for prevention of enzymic inactivation of pharmaceuticals)

IT Drug bioavailability
(of proteolytically-labile pharmaceuticals, proteins and peptides for enhancement of)

IT Fish
(proteins of, for prevention of enzymic inactivation of pharmaceuticals)

IT Almond
Peanut
Soybean
(flour, proteins and peptides from, for prevention of enzymic inactivation of pharmaceuticals)

IT Lymphokines and Cytokines
RL: PROC (Process)
(interleukins, enzymic protection of, in pharmaceuticals, with peptides and proteins)

IT 50-56-6, **Oxytocin**, biological studies 1393-25-5, Secretin 1947-37-1, Tetragastrin 5534-95-2, Pentagastrin 9002-60-2, Adrenocorticotropin, biological studies 9002-62-4, Prolactin, biological studies 9002-68-0, Follicle stimulating hormone 9002-71-5, Thyrotropin 9002-72-6, Growth hormone 9002-76-0, Gastrin 9004-10-8, Insulin, biological studies 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 9011-97-6, Cholecystokinin 9034-40-6, Luteinizing hormone-releasing factor 11000-17-2, Vasopressin 33507-63-0, Substance p 39379-15-2, Neurotensin 53714-56-0, Leuprolide 69558-55-0, Thymopentin 116243-73-3, Endothelin 118549-37-4, Insulinotropin 119625-78-4, Terlakiren
RL: BIOL (Biological study)

(enzymic protection of, in pharmaceuticals, with proteins and peptides)
IT 9001-12-1, Collagenase 9001-75-6, Pepsin 9002-07-7, Trypsin
9004-06-2, Elastase 9004-07-3, Chymotrypsin 9031-94-1, Aminopeptidase
9031-98-5, Carboxypeptidase
RL: BIOL (Biological study)
(inactivation of pharmaceuticals by, prevention of, with proteins and peptides)

L14 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:17074 HCAPLUS
DN 118:17074
ED Entered STN: 24 Jan 1993
TI Analysis of cis-acting elements of **oxytocin** gene by DNA-mediated gene transfer
AU Richard, Stephane; Zingg, Hans H.
CS **Pfizer** Cent. Res., Groton, CT, 06340, USA
SO Methods in Neurosciences (1992), 9(Gene Expression Neural Tissues), 324-43
CODEN: MENEE5; ISSN: 1043-9471
DT Journal
LA English
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 2
AB Techniques pertaining to the anal. of promoter function by transient expression of chimeric gene constructs using the hypothalamic nonapeptide oxytocin (OT) gene as a model system are described. Specifically, the authors describe (1) promoter/reporter gene construction, (2) transfection techniques, and (3) modification of promoter sequences by 5' or 3' deletions and site-directed mutagenesis. Moreover, a novel version of a protocol for site-directed mutagenesis using the polymerase chain reaction (PCR) technique is described.
ST **oxytocin** promoter analysis gene transfer
IT Gene, animal
RL: BIOL (Biological study)
(for **oxytocin**, promoter anal. of, DNA-mediated gene transfer for)
IT Transformation, genetic
(**oxytocin** gene promoter anal. using)
IT Genetic element
RL: BIOL (Biological study)
(promoter, of **oxytocin** gene, DNA-mediated gene transfer for anal. of)
IT 50-56-6, **Oxytocin**, biological studies
RL: BIOL (Biological study)
(promoter of gene for, DNA-mediated gene transfer in anal. of)

=> b home
FILE 'HOME' ENTERED AT 08:09:01 ON 28 JUL 2004

=> b reg
FILE 'REGISTRY' ENTERED AT 10:11:02 ON 28 JUL 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 27 JUL 2004 HIGHEST RN 717822-84-9
DICTIONARY FILE UPDATES: 27 JUL 2004 HIGHEST RN 717822-84-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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conducting SmartSELECT searches.

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Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide 140

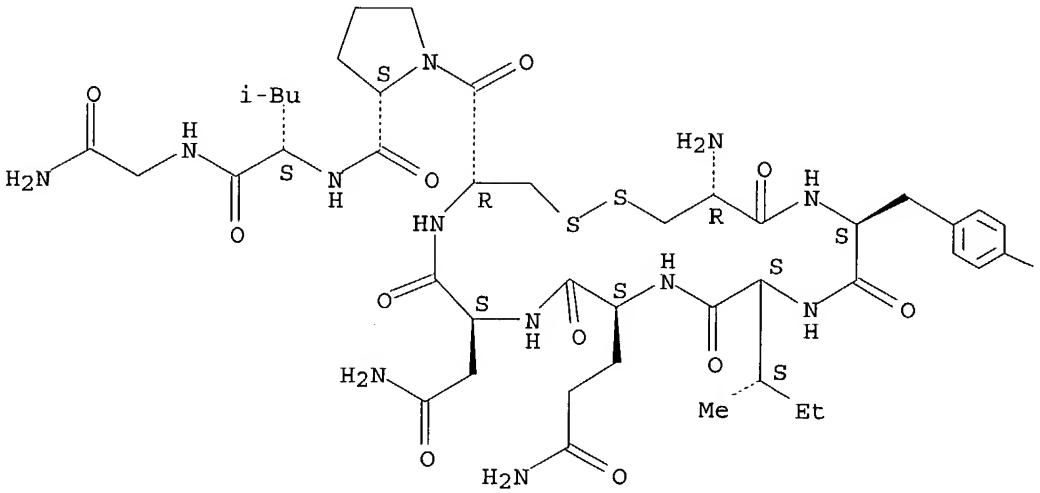
L40 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **50-56-6** REGISTRY
CN Oxytocin (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,2-Dithia-5,8,11,14,17-pentaazacycloeicosane, cyclic peptide deriv.
OTHER NAMES:
CN .alpha.-Hypophamine
CN 1: PN: WO0178758 SEQID: 1 claimed protein
CN 1: PN: WO2004000993 PAGE: 53 claimed protein
CN 3-Isoleucine-8-leucine vasopressin
CN Alpha-hypophamine
CN Atonin O
CN Atonin O, 3-L-isoleucine-8-L-leucine-
CN Di-sipidin
CN Endopituitrina
CN Glycinamide, L-cysteinyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-L-prolyl-L-leucyl-, cyclic (1.fwdarw.6)-disulfide
CN Hyphotocin
CN Intertocine S
CN L-Cysteinyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-L-prolyl-L-leucylglycinamide cyclic (1.fwdarw.6)-disulfide
CN Nobitocin S
CN Orasthin
CN Oxystin
CN Partocon
CN Perlacton
CN Pitocin
CN Piton S
CN Presoxin
CN Synpitan
CN Synpitan forte
CN Synthetic oxytocin
CN Syntocin
CN Syntocinon

CN Syntocinone
CN Uteracon
CN Vasopressin, 3-L-isoleucine-8-L-leucine-
CN [1-Hemicystine]-oxytocin
FS PROTEIN SEQUENCE; STEREOSEARCH
DR 112457-76-8, 147207-13-4
MF C43 H66 N12 O12 S2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



Searched by Noble Jarrell

PAGE 1-B

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11101 REFERENCES IN FILE CA (1907 TO DATE)
322 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
11117 REFERENCES IN FILE CAPLUS (1907 TO DATE)
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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STRUCTURE FILE UPDATES: 27 JUL 2004 HIGHEST RN 717822-84-9
DICTIONARY FILE UPDATES: 27 JUL 2004 HIGHEST RN 717822-84-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L40 123 SEA FILE=REGISTRY ABB=ON PLU=ON L39 AND OXYTOCIN
L41 113 SEA FILE=REGISTRY ABB=ON PLU=ON L40 NOT ((PMS OR IDS OR MAN)/CI OR UNPSECIFIED OR COMPD OR COMPOUND)
L42 11298 SEA FILE=HCAPLUS ABB=ON PLU=ON L38 OR L41
L44 15163 SEA FILE=HCAPLUS ABB=ON PLU=ON ?OXYTOCIN?/BI
L45 17 SEA FILE=HCAPLUS ABB=ON PLU=ON ALPHA/OBI (1A) HYPOPHAMINE/OBI OR ATONIN O/OBI OR DI/OBI (1A) SIPIDIN/OBI OR ENDOPITUITRINA/OBI OR HYPHOTOCIN/OBI OR (INTERTOCINE/OBI OR NOBITOCIN#/OBI)(W)S/OBI OR ORASTHIN#/OBI OR OSYSTIN#/OBI OR PARTOCON#/OBI
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Searched by Noble Jarrell

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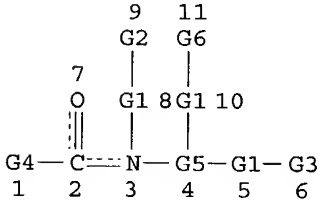

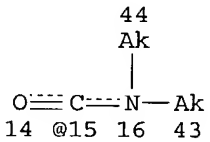

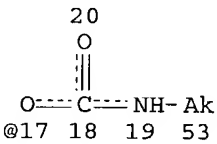

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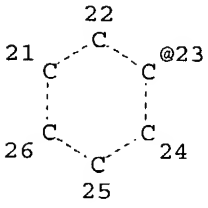

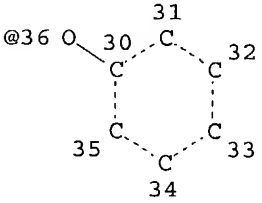

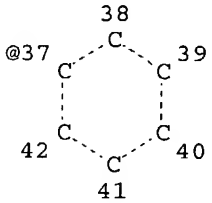

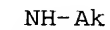

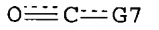

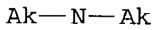

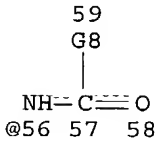

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GGCAT IS UNS AT 27
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 21 30
NUMBER OF NODES IS 57

STEREO ATTRIBUTES: NONE

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SEARCH TIME: 00.00.01

Searched by Noble Jarrell

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                E BELL A/AU
L2          144 E3,E32-33
                E BELL ANDREW/AU
L3          100 E3,E13-14
                E EDWARS P/AU
                E EDWARDS P/AU
L4           98 E3,E11,E45-46
                E ELLIS D/AU
L5          196 E3,E45
                E HEPWORTH D/AU
L6           25 E3-6
                E LEWIS M/AU
L7          131 E3,E20,E83-84
                E SMITH C/AU
L8          422 E3
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L9          160 E3-6
                E SMITH CHRISTPHER/AU
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L10         108 E3,E39-40
L11       10834 PFIZER/CS,PA
L12           2 L1-10 AND OXYTOCIN
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L14           6 L13 NOT L12

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L19         523 L16 OR L18
L20             STR
L21             STR L20
L22          24 L21
L23             SCR 2039 OR 2041 OR 2050 OR 2049 OR 2048 OR 2053 OR 2052 OR 204
L24          18 L21 NOT L23
L25             STR L21
L26           3 L25
L27             SCR 2087
L28           5 L25 AND L27 NOT L23
L29             STR L25
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L31           2 L29 AND L27 NOT L23
L32             STR L29
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L39         129 C43H66N12O12S2
L40         123 L39 AND OXYTOCIN
L41         113 L40 NOT ((PMS OR IDS OR MAN)/CI OR UNPSECIFIED OR COMPD OR COMP

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L59           1 L57-58
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L65           7 L60 AND P/DT
L66          30 L60 NOT (NMR OR CIRCULAR DICHROISM)/TI
L67           4 L60 NOT L66
L68          29 L66 NOT (HSQC-TOCSY)/TI
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FILE COVERS 1907 - 28 Jul 2004  VOL 141 ISS 5
FILE LAST UPDATED: 27 Jul 2004  (20040727/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L68  ANSWER 1 OF 29  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:696912  HCAPLUS
DN   139:214723
ED   Entered STN:  05 Sep 2003
TI   Intermediates and methods for making heptapeptide oxytocin analogs
IN   Wisniewski, Kazimerz; Stalewski, Jacek; Jiang, Guancheng
PA   Ferring BV, Neth.
SO   PCT Int. Appl., 32 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  C07K001-00
CC   34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 1
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PI   WO 2003072597      A1   20030904       WO 2003-US4301   20030213
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
             ML, MR, NE, SN, TD, TG
PRAI US 2002-360345P   P   20020227
OS   MARPAT 139:214723
GI
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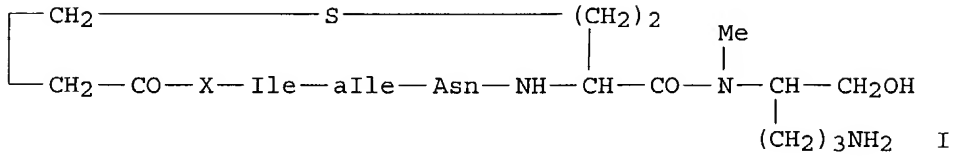


I

AB More efficient and/or economical methods for synthesizing heptapeptide alc. analogs of oxytocin are provided along with novel intermediates which are useful in synthesizing such oxytocin analogs. Intermediates P1-NRCH(CH2O-W)(CH2)nNP2P3 [P1 is H or an amino-protecting group; P2 and P3 are amino-protecting groups that are different from P1 and are not labile under conditions that would remove P1, provided that P2 and P3 may be a divalent amino-protecting group; n is 2, 3 or 4; R is lower alkyl; W is H, a protecting group or resin] are claimed. Thus, peptides I (X = D-Nal, D-Trp; claimed compds.) were prepared by the solid-phase method and assayed for oxytocin receptor binding. Peptide I (X = D-Nal) showed Ki = 0.1 nM, which is considered to be excellent.

ST peptide alc analog oxytocin prepn

IT Solid phase synthesis
(peptide; synthesis of heptapeptide alc. analogs of oxytocin)

IT Muscle
(uterine; blocking of contractions by heptapeptide alc. analogs of oxytocin)

IT 181370-86-5P
RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of heptapeptide alc. analogs of oxytocin)

IT 50-56-6DP, Oxytocin, analogs **208400-64-0P 285571-64-4P 344428-67-7P 586964-41-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of heptapeptide alc. analogs of oxytocin)

IT 63-68-3, L Methionine, reactions 1663-39-4, tert-Butyl acrylate 3304-51-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of heptapeptide alc. analogs of oxytocin)

IT 5874-56-6P 95824-70-7P 98441-66-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of heptapeptide alc. analogs of oxytocin)

IT 586964-38-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of heptapeptide alc. analogs of oxytocin)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Albert; US 5656721 A 1997 HCAPLUS

(2) Obiols; US 6346601 B1 2002 HCAPLUS

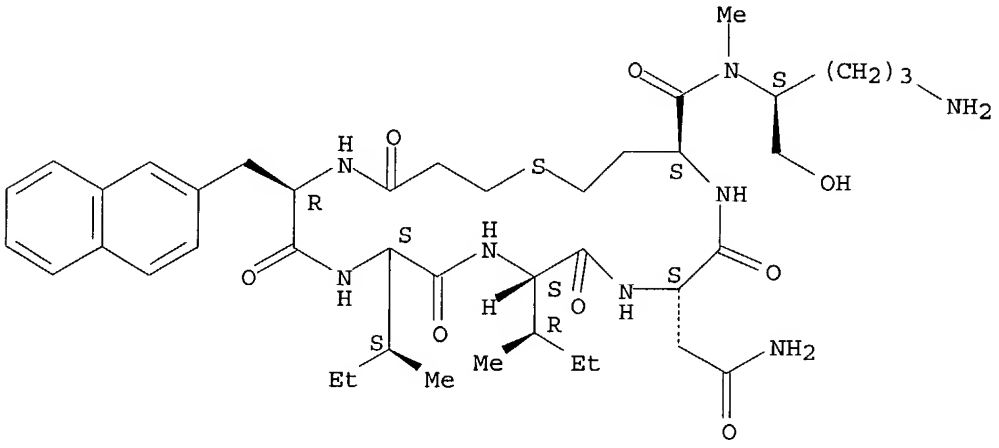
IT **208400-64-0P 285571-64-4P 344428-67-7P 586964-41-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of heptapeptide alc. analogs of oxytocin)

RN 208400-64-0 HCAPLUS

CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-

L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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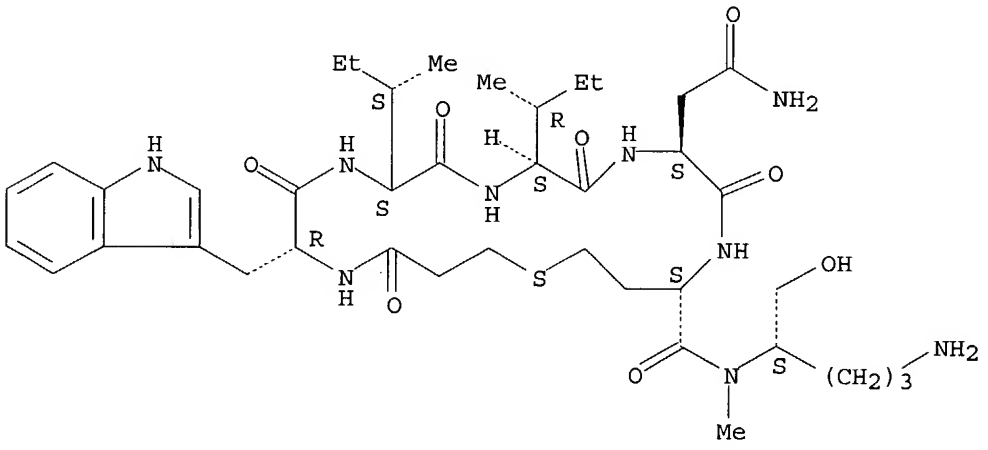
Absolute stereochemistry.



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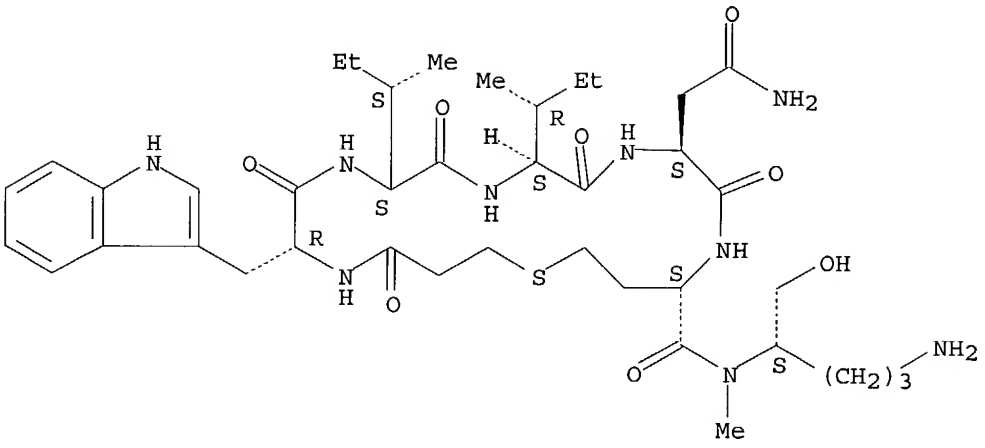
CRN 285571-64-4
CMF C40 H63 N9 O8 S

Absolute stereochemistry.



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CRN 76-05-1
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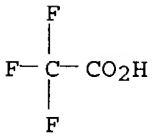

RN 586964-41-2 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 208400-64-0
CMF C42 H64 N8 O8 S

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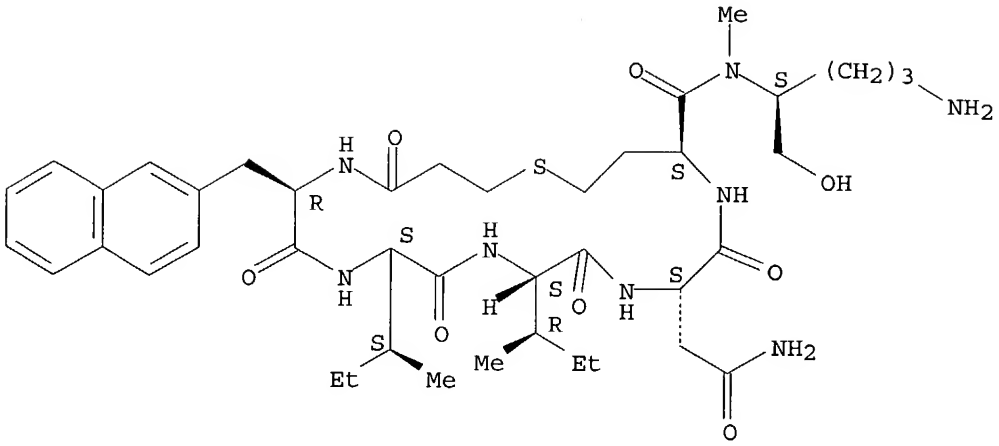

CM 2

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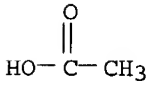
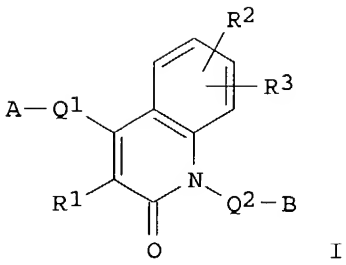
CMF C2 H4 O2



L68 ANSWER 2 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:389980 HCAPLUS
DN 138:401612
ED Entered STN: 21 May 2003
TI Preparation of carbostyryl derivatives and their use as oxytocin antagonists and therapeutics for treatment of premature delivery, miscarriage, dysmenorrhea, and galactorrhea
IN Shiraiwa, Masafumi; Ota, Shuji; Takefuchi, Ken; Uchida, Hiroshi; Saegusa, Mamoru; Mitsubori, Tomohiro; Yoshizawa, Masayuki
PA Teikoku Hormone Mfg. Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 142 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07D215-22
ICS A61K031-439; A61K031-4704; A61K031-4709; A61K031-4725; A61K031-496; A61K031-506; A61K031-5377; A61K031-55; A61K031-551; A61P015-00; A61P015-06; C07D215-50; C07D401-04; C07D401-06; C07D401-12; C07D401-14; C07D405-04; C07D405-06; C07D405-14
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003146972	A2	20030521	JP 2001-348850	20011114

PRAI JP 2001-348850 20011114
OS MARPAT 138:401612
GI



I

AB Title derivs. I [Q1 = bond, CH2, CH2CH2, vinyl, CHMe, etc.; A = lower alkyl, (un)substituted cycloalkyl (condensed with hydrocarbyl ring), (un)substituted aryl, (un)substituted heterocyclyl (condensed with hydrocarbyl ring); R1 = H, lower alkyl; R2, R3 = H, (un)substituted lower alkyl(oxy), aralkyloxy, piperidinyl, etc.; R2R3 may be linked to form lower alkylenedioxy; Q2 = bond, CH2, CH2CH2, etc.; B = CO2H, lower alkoxycarbonyl, (un)substituted 2-pyridinyl, (un)substituted Ph, (un)substituted cyclohexyl, etc.] or their salts are claimed. The derivs. are also useful for termination of delivery prior to Caesarean section. Thus, 4-(2,3-dimethoxyphenyl)-7-methoxy-2-oxoquinoline was treated with Me 4-bromomethylbenzoate to give 56% I (AQ1 = 2,3-dimethoxyphenyl, R1-R3 = H, Q2B = 4-CH2C6H4CO2Me), which inhibited binding of [3H]-oxytocin to its receptor with IC50 of 0.972 .mu.mol/L.

ST oxytocin antagonist carbostyryl prepn; premature delivery miscarriage treatment carbostyryl prepn; dysmenorrhea galactorrhea treatment carbostyryl prepn; Caesarean section oxytocin antagonist carbostyryl prepn

IT Parturition
(Caesarean; preparation of carbostyryl derivs. as oxytocin antagonists)

IT Lactation
(galactorrhea, treatment of; preparation of carbostyryl derivs. as oxytocin antagonists)

IT Parturition
(premature, treatment of; preparation of carbostyryl derivs. as oxytocin antagonists)

IT Oxytocin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of carbostyryl derivs. as oxytocin antagonists)

IT Abortion
(spontaneous, treatment of; preparation of carbostyryl derivs. as oxytocin antagonists)

IT Dysmenorrhea
(treatment of; preparation of carbostyryl derivs. as oxytocin antagonists)

IT 528820-01-1P 528820-25-9P 528820-77-1P 528820-83-9P 528821-37-6P
528821-49-0P 528822-96-0P 528824-97-7P 528827-39-6P 528828-66-2P
528828-67-3P 528828-76-4P 528829-39-2P 528829-68-7P 528830-73-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of carbostyryl derivs. as oxytocin antagonists)

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carbostyryl derivs. as oxytocin antagonists)

IT 528821-91-2P 528821-92-3P 528821-93-4P 528821-94-5P 528821-96-7P
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528823-22-5P 528823-23-6P **528823-24-7P 528823-25-8P**
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528824-54-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of carbostyryl derivs. as oxytocin antagonists)

IT 528824-55-7P 528824-56-8P 528824-57-9P 528824-58-0P 528824-59-1P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carbostyryl derivs. as oxytocin antagonists)

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528828-72-0P 528828-73-1P 528828-74-2P 528828-75-3P 528828-77-5P
528828-78-6P 528828-79-7P 528828-80-0P 528828-81-1P 528828-82-2P
528828-83-3P 528828-84-4P 528828-85-5P 528828-86-6P 528828-91-3P
528828-93-5P 528828-94-6P 528828-95-7P 528828-96-8P 528828-97-9P
528828-98-0P 528828-99-1P 528829-00-7P 528829-01-8P 528829-02-9P
528829-03-0P 528829-04-1P 528829-05-2P 528829-06-3P 528829-07-4P
528829-08-5P 528829-09-6P 528829-12-1P 528829-13-2P 528829-14-3P
528829-15-4P 528829-16-5P 528829-17-6P 528829-18-7P 528829-19-8P

528829-20-1P 528829-21-2P 528829-22-3P 528829-23-4P 528829-24-5P
528829-25-6P 528829-26-7P 528829-27-8P 528829-28-9P 528829-29-0P
528829-30-3P 528829-31-4P 528829-33-6P 528829-34-7P 528829-35-8P
528829-37-0P 528829-38-1P 528829-40-5P 528829-42-7P 528829-44-9P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carbostyryl derivs. as oxytocin antagonists)

IT 528830-10-6P 528830-12-8P 528830-13-9P 528830-14-0P 528830-15-1P
528830-16-2P 528830-17-3P 528830-18-4P 528830-19-5P 528830-20-8P
528830-21-9P 528830-22-0P 528830-23-1P 528830-24-2P 528830-25-3P
528830-26-4P 528830-27-5P 528830-28-6P 528830-29-7P 528830-30-0P
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528830-46-8P 528830-47-9P 528830-48-0P 528830-49-1P 528830-50-4P
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528830-61-7P 528830-62-8P 528830-63-9P 528830-64-0P 528830-65-1P
528830-66-2P 528830-67-3P 528830-68-4P 528830-69-5P 528830-70-8P
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528830-97-9P 528838-55-3P 528838-56-4P 528854-42-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carbostyryl derivs. as oxytocin antagonists)

IT 528819-92-3 528819-94-5 528820-31-7 528821-55-8 528821-95-6
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528822-84-6 528822-85-7 528822-86-8 528822-87-9 528822-88-0
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528826-70-2 528826-84-8 528826-85-9 528826-91-7 528826-99-5
528827-00-1 528827-09-0 528827-10-3 528827-15-8 528827-16-9
528827-25-0 528827-26-1 528827-29-4 528827-33-0 528827-63-6
528827-64-7 528827-70-5 528827-71-6 528827-75-0 528827-79-4
528827-80-7 528827-85-2 528827-86-3 528827-89-6 528827-90-9
528827-98-7 528827-99-8 528828-00-4 528828-87-7 528828-88-8
528828-89-9 528829-10-9 528829-11-0 528829-76-7 528830-11-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of carbostyryl derivs. as oxytocin antagonists)

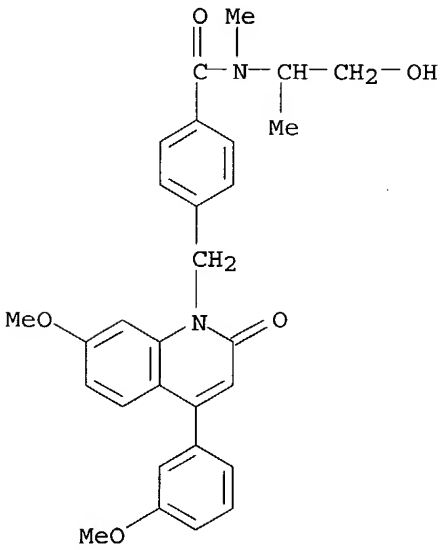
IT 59-67-6, Nicotinic acid, reactions 79-44-7, N,N-Dimethylcarbamoyl chloride 94-02-0, Ethyl benzoylacetate 96-32-2, Bromoacetic acid

methyl ester 100-11-8, 4-Nitrobenzyl bromide 100-39-0, Benzyl bromide 105-36-2, Ethyl bromoacetate 107-30-2, Methoxymethyl chloride 122-59-8, Phenoxyacetic acid 350-46-9, 4-Fluoronitrobenzene 462-08-8, 3-Aminopyridine 503-66-2, 3-Hydroxypropionic acid 536-90-3, m-Anisidine 553-03-7 586-37-8 616-38-6, Dimethyl carbonate 1521-38-6, 2,3-Dimethoxybenzoic acid 2417-72-3, 4-Bromomethylbenzoic acid methyl ester 3303-84-2 4530-20-5 5798-75-4, Ethyl 4-bromobenzoate 15733-89-8 15761-39-4 25503-90-6, 1-Acetylpiperidine-4-carboxylic acid 26116-12-1, (1-Ethyl-2-pyrrolidinyl)methylamine 37517-78-5, Monoethyl malonate magnesium salt 57260-73-8 109384-19-2, 1-tert-Butyloxycarbonyl-4-hydroxypiperidine 150356-53-9 528831-12-1 528831-14-3 528831-16-5 528831-18-7 528831-19-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of carbostyryl derivs. as oxytocin antagonists)

IT 779-81-7P 23058-90-4P 30034-41-4P 30034-43-6P 41051-18-7P 81745-20-2P 81745-21-3P 528830-98-0P 528830-99-1P 528831-00-7P 528831-01-8P 528831-02-9P 528831-03-0P 528831-04-1P 528831-05-2P 528831-06-3P 528831-07-4P 528831-08-5P 528831-09-6P 528831-10-9P 528831-11-0P 528831-13-2P 528831-15-4P 528831-17-6P 528831-20-1P 528831-21-2P 528831-22-3P 528831-23-4P 528831-24-5P 528831-25-6P, 7-Methoxy-2-(4-nitrophenoxy)-4-phenylquinoline 528831-26-7P 528831-27-8P 528831-28-9P 528831-29-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbostyryl derivs. as oxytocin antagonists)

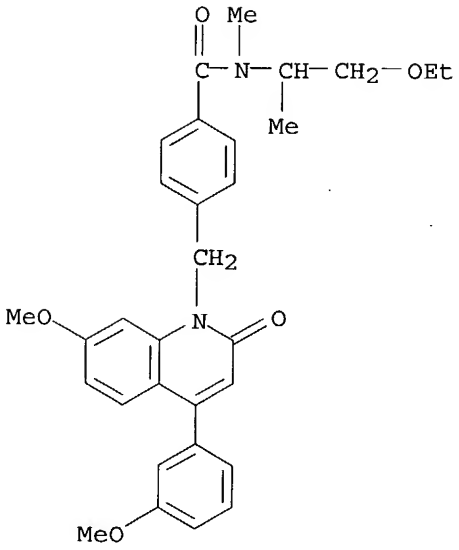
IT **528823-24-7P 528823-25-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carbostyryl derivs. as oxytocin antagonists)

RN 528823-24-7 HCAPLUS
CN Benzamide, N-(2-hydroxy-1-methylethyl)-4-[[7-methoxy-4-(3-methoxyphenyl)-2-oxo-1(2H)-quinolinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



RN 528823-25-8 HCAPLUS
CN Benzamide, N-(2-ethoxy-1-methylethyl)-4-[[7-methoxy-4-(3-methoxyphenyl)-2-

oxo-1(2H)-quinolinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



L68 ANSWER 3 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:814138 HCAPLUS
DN 137:325440
ED Entered STN: 25 Oct 2002
TI Preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists
IN Failli, Amedeo Arturo; Shumsky, Jay Scott; Caggiano, Thomas Joseph; Sabatucci, Joseph Peter; Memoli, Kevin Anthony; Trybulski, Eugene John; Sanders, William Jennings
PA Wyeth, John, and Brother Ltd., USA
SO PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D487-04
ICS C07D471-14; A61K031-5517; A61P015-06
CC 28-21 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002083680	A1	20021024	WO 2002-US11530	20020411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003018026	A1	20030123	US 2002-120100	20020410
EP 1377583	A1	20040107	EP 2002-728748	20020411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2001-283261P P 20010412
WO 2002-US11530 W 20020411
OS MARPAT 137:325440
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; ring containing Z = II, III (wherein R1, R2 = H, alkyl, halo, etc.); R3 = H, alkyl, alkoxy, etc.; R4 = BC (B = IV, V; C = (un)substituted Ph, 1-naphthyl, 1-pyrrolyl, etc.; A = CH, N; R5-R7 = H, alkyl, alkoxy, etc.)] which act as oxytocin receptor competitive antagonists, and therefore are useful in treatment, inhibition, suppression or prevention of preterm labor, dysmenorrhea and endometritis, suppression of labor at term prior to Caesarian delivery, and to facilitate antinatal transport to a medical facility, were prepared E.g., a 7-step synthesis of VI which showed IC50 of 1.37 nM against human oxytocin receptor binding (CHO cell line), was given. The compds. I are also useful in enhancing fertility rates, enhancing survival rates and synchronizing estrus in farm animals, and may be useful in the prevention and treatment of disfunctions of the oxytocin system in the central nervous system including obsessive compulsive disorder (OCD) and neuropsychiatric disorders.

ST tricyclic benzodiazepine carboxamide prepn tocolytic oxytocin receptor antagonist; pyrrolobenzodiazepinecarboxamide prepn preterm labor dysmenorrhea endometritis uterine relaxant

IT Uterus, disease
(endometritis, treatment of; preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)

IT Mental disorder
(obsession-compulsion, treatment of; preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)

IT Parturition
(premature, treatment of; preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)

IT Fertility
Human
Tocolytic agents
(preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)

IT Oxytocin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)

IT Parturition
(preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists for suppressing labor prior to Caesarian delivery)

IT Dysmenorrhea
Mental disorder
(treatment of; preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)

IT 473610-07-0P 473610-10-5P 473610-27-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of novel tricyclic benzodiazepine carboxamides as tocolytic

oxytocin receptor antagonists)

IT 473610-06-9P 473610-08-1P 473610-11-6P 473610-12-7P 473610-14-9P
473610-16-1P 473610-19-4P 473610-20-7P 473610-22-9P 473610-23-0P
473610-25-2P 473610-28-5P 473610-30-9P 473610-32-1P 473610-33-2P
473610-35-4P 473610-37-6P 473610-38-7P 473610-40-1P 473610-42-3P
473610-45-6P 473610-46-7P 473610-48-9P 473610-50-3P 473610-52-5P
473610-53-6P 473610-54-7P 473610-55-8P 473610-56-9P
473610-58-1P 473610-60-5P 473610-62-7P 473610-64-9P
473610-66-1P 473610-67-2P 473610-69-4P 473610-72-9P 473610-74-1P
473610-75-2P 473610-77-4P 473610-79-6P 473610-80-9P 473610-82-1P
473610-84-3P 473610-86-5P 473610-88-7P 473610-90-1P 473610-91-2P
473610-93-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)

IT 77-86-1, 2-Amino-2-hydroxymethyl-1,3-propanediol 100-51-6, Benzyl alcohol, reactions 103-76-4, 1-(2-Hydroxyethyl)piperazine 121-33-5, Vanillin 619-42-1, Methyl 4-bromobenzoate 1003-29-8, Pyrrole-2-carboxaldehyde 1423-27-4, 2-Trifluoromethylphenylboronic acid 1692-15-5, Pyridine-4-boronic acid 1993-03-9, 2-Fluorophenylboronic acid 3900-89-8, 2-Chlorophenylboronic acid 5720-06-9, 2-Methoxyphenylboronic acid 6284-40-8, N-Methyl-D-glucamine 7115-46-0 7206-70-4, 4-Amino-5-chloro-2-methoxybenzoic acid 7697-28-1, 4-Bromo-3-methylbenzoic acid 13484-40-7 13922-41-3, 1-Naphthaleneboronic acid 14618-80-5 16419-60-6, 2-Methylphenylboronic acid 21900-25-4 22162-53-4, 10,11-Dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine 23356-96-9, (S)-2-Pyrrolidinemethanol 27492-84-8, Methyl 4-amino-2-methoxybenzoate 34569-34-1 35458-39-0 40137-22-2, 3-(Methylamino)-1,2-propanediol 53413-67-5, 4,5-Dimethoxy-2-nitrobenzyl bromide 57260-71-6, 1-(tert-Butoxycarbonyl)piperazine 58757-38-3, 6-Chloronicotinoyl chloride 59748-90-2, 4-Bromo-2-chlorobenzoic acid 60456-23-7, (S)-Glycidol 64491-68-5, (S)-Glycidyl methyl ether 64491-70-9 65719-09-7, Methyl 2-methylnicotinate 213211-69-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)

IT 53413-62-0P 53478-80-1P 89942-34-7P 106359-69-7P 148490-97-5P
148547-19-7P 177785-14-7P 179408-52-7P 194018-68-3P 220461-97-2P
229467-26-9P 473260-51-4P 473260-56-9P 473260-57-0P 473260-59-2P
473260-60-5P 473260-62-7P 473260-70-7P 473260-72-9P 473260-73-0P
473260-74-1P 473260-78-5P 473260-79-6P 473260-80-9P 473260-83-2P
473260-86-5P 473260-87-6P 473263-99-9P 473264-00-5P 473264-01-6P
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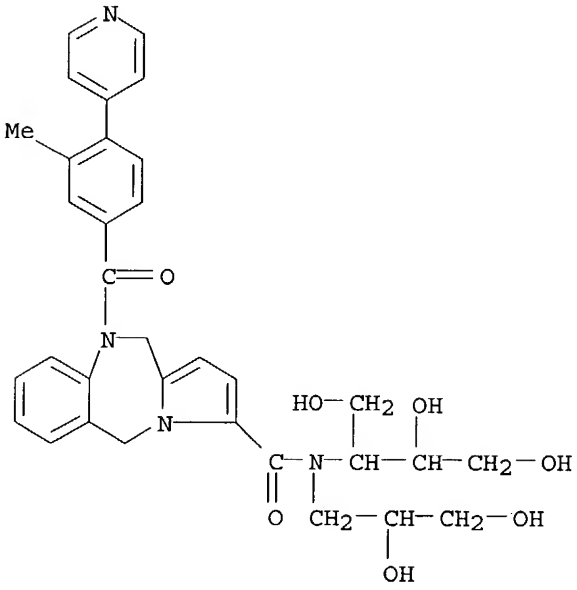
473264-07-2P 473264-08-3P 473264-09-4P 473264-10-7P 473264-11-8P
473264-13-0P 473264-14-1P 473264-15-2P 473264-16-3P 473264-17-4P
473264-19-6P 473264-20-9P 473264-21-0P 473264-22-1P 473264-23-2P
473264-28-7P 473264-29-8P 473264-31-2P 473264-32-3P 473264-35-6P
473264-36-7P 473476-78-7P 473476-80-1P 473476-81-2P 473611-05-1P
473611-09-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) American Home Prod; WO 9906409 A 1999 HCAPLUS
(2) Caggiano, T; US 5880122 A 1999 HCAPLUS
(3) Venkatesan, A; US 5521173 A 1996 HCAPLUS

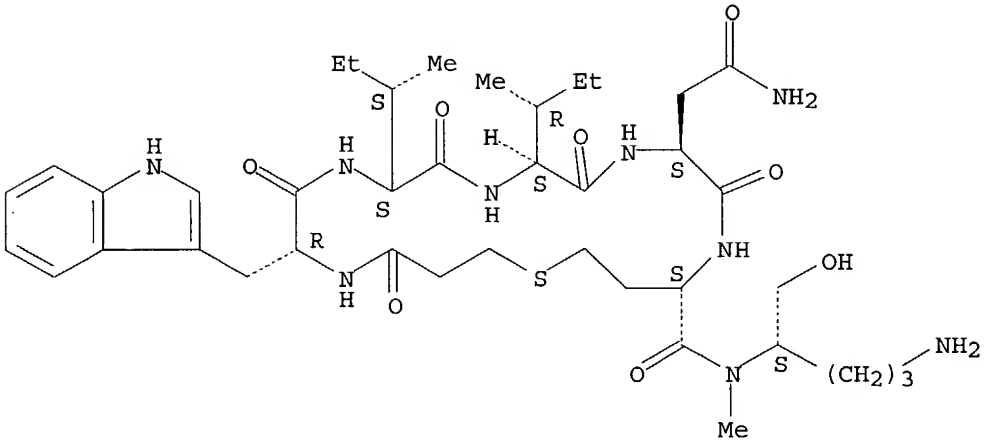
IT **473610-58-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)
RN 473610-58-1 HCAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide, N-[2,3-dihydroxy-1-(hydroxymethyl)propyl]-N-(2,3-dihydroxypropyl)-10,11-dihydro-10-[3-methyl-4-(4-pyridinyl)benzoyl]- (9CI) (CA INDEX NAME)



L68 ANSWER 4 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:288596 HCAPLUS
DN 133:120653
ED Entered STN: 04 May 2000
TI In search for a new class of oxytocin antagonists
AU Wisniewski, Kazimierz; Trojnar, Jerzy; Haigh, Robert; Yea, Chris; Ashworth, Doreen; Melin, Per; Nilsson, Anders
CS Ferring Research Institute, San Diego, CA, 92121, USA
SO Peptides 1998, Proceedings of the European Peptide Symposium, 25th, Budapest, Aug. 30-Sept. 4, 1998 (1999), Meeting Date 1998, 518-519. Editor(s): Bajusz, Sandor; Hudecz, Ferenc. Publisher: Akademiai Kiado, Budapest, Hung.
CODEN: 68WKAY
DT Conference
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
AB A symposium report. Several analogs of the potent oxytocin antagonist F792 have been designed and synthesized. In general, in vivo potency of the analogs paralleled the affinity for the human oxytocin receptor.
ST cyclic peptide analog F792 prepn oxytocin antagonist symposium
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological

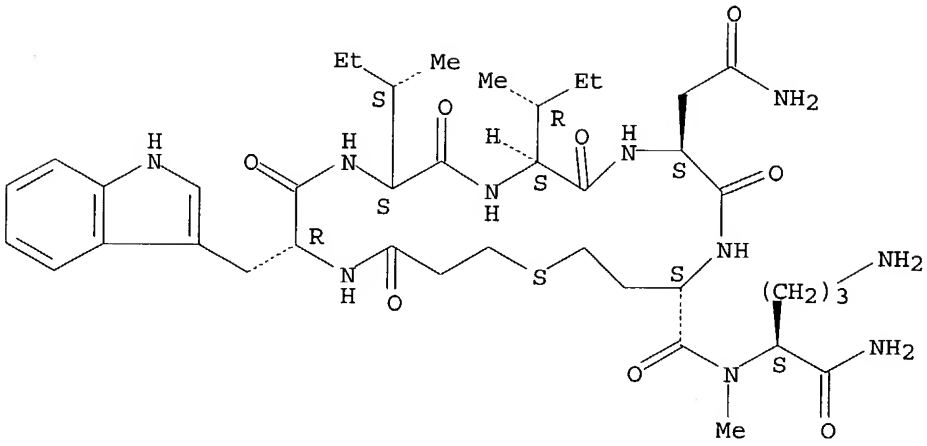
study); PREP (Preparation)
(cyclic; synthesis of peptides as oxytocin antagonists)
IT Structure-activity relationship
(oxytocin-inhibiting; synthesis of peptides as oxytocin antagonists)
IT 252940-51-5P 252940-52-6P 252940-53-7P 252940-54-8P 252940-55-9P
285571-64-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of peptides as oxytocin antagonists)
IT 50-56-6, Oxytocin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(synthesis of peptides as oxytocin antagonists)
IT **176742-08-8P**, f792
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of peptides as oxytocin antagonists)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Barlos, K; Int J Peptide Protein Res 1991, V37, P513 HCAPLUS
(2) Nilsson, A; Peptides 1996 1997, P683
(3) Volante, R; Tetrahedron Lett 1981, V22, P3119 HCAPLUS
(4) Wisniewski, K; J Peptide Sci 1998, V4, P1 HCAPLUS
IT **285571-64-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of peptides as oxytocin antagonists)
RN 285571-64-4 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **176742-08-8P**, f792
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of peptides as oxytocin antagonists)
RN 176742-08-8 HCAPLUS
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L68 ANSWER 5 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:662314 HCAPLUS
DN 132:50242
ED Entered STN: 18 Oct 1999
TI The synthesis of a new class of oxytocin antagonists
AU Wisniewski, Kazimierz; Trojnar, Jerzy; Riviere, Pierre; Haigh, Robert; Yea, Chris; Ashworth, Doreen; Melin, Per; Nilsson, Anders
CS Ferring Research Institute, San Diego, CA, 92121, USA
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(19), 2801-2804
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2
OS CASREACT 132:50242
AB The synthesis of a new class of oxytocin antagonists, with significantly modified C-terminal part, is described. The chemical of the Mitsunobu reaction was applied to obtain the key derivs. In spite of the extensive modifications of previously described compound F792, the peptides retain biol. activity as oxytocin antagonists.
ST peptide oxytocin antagonist prepn Mitsunobu reaction acetylthiol
IT Dehydration reaction
(Mitsunobu reaction; synthesis of S-acetylthiols as intermediates in preparing a new class of oxytocin antagonists using)
IT Enzyme kinetics
(synthesis of a new class of oxytocin antagonists)
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of a new class of oxytocin antagonists)
IT 50-56-6, Oxytocin, properties
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(antagonists; preparation and biol. activity of as a new class of oxytocin antagonists using a Mitsunobu reaction)
IT **176742-08-8**, f 792

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(biol. activity of as oxytocin antagonist)

IT 252940-51-5P 252940-52-6P 252940-53-7P 252940-54-8P 252940-55-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of as a new class of oxytocin antagonists using a Mitsunobu reaction)

IT 105562-75-2P 233689-90-2P 252940-35-5P 252940-36-6P 252940-37-7P
252940-38-8P 252940-39-9P 252940-40-2P 252940-41-3P 252940-42-4P
252940-43-5P 252940-44-6P 252940-45-7P 252940-46-8P 252940-47-9P
252940-48-0P 252940-49-1P 252940-50-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of in the synthesis of a new class of oxytocin antagonists using a Mitsunobu reaction)

IT 507-09-5, Thiolacetic acid, reactions 2480-93-5 16937-92-1
55878-47-2 110661-91-1, tert-Butyl 4-bromobutyrate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of in the synthesis of a new class of oxytocin antagonists using a Mitsunobu reaction)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

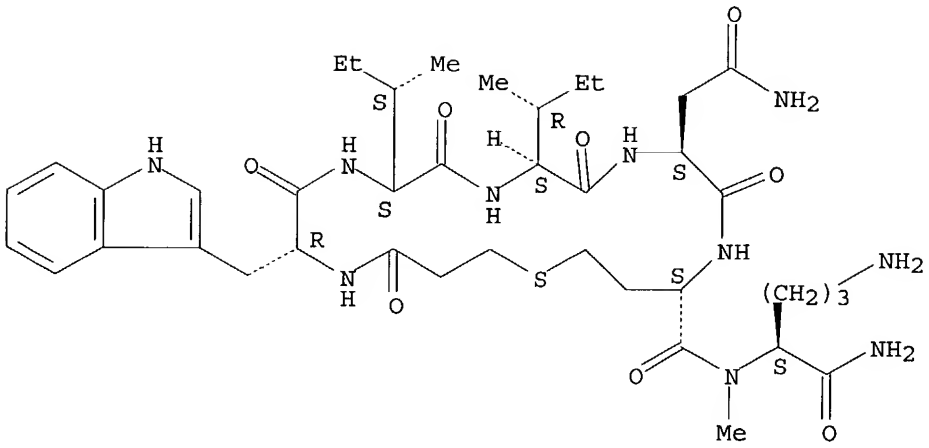
(1) Aurell, C; WO 95/02609 1995 HCAPLUS
(2) Barlos, K; J Peptide Protein Res 1991, V37, P513 HCAPLUS
(3) Bolin, D; Int J Peptide Protein Res 1989, V33, P353 HCAPLUS
(4) Cheng, Y; Biochem Pharmacol 1973, V22, P3099 HCAPLUS
(5) Fujii, N; Chem Pharm Bull 1987, V35, P3880 HCAPLUS
(6) Jost, K; Handbook of Neurohypophyseal Hormone Analogs 1987, V1(2), P144
(7) Kimura, T; Nature 1992, V356, P526 HCAPLUS
(8) Melin, P; J Endocrinol 1981, V88, P173 HCAPLUS
(9) Melin, P; J Endocrinol 1986, V111, P125 HCAPLUS
(10) Melin, P; Peptides: Structure and Function (Proceedings of the 8th American Peptide Symposium) 1983, P361 HCAPLUS
(11) Mitsunobu, O; Synthesis 1981, P1 HCAPLUS
(12) Nilsson, A; Peptides 1996 (Proceedings of the 24th European Peptide Symposium) 1997, P683
(13) Rodriguez, M; Tetrahedron Lett 1991, V32, P923 HCAPLUS
(14) Volante, R; Tetrahedron Lett 1981, V22, P3119 HCAPLUS
(15) Wisniewski, K; J Peptide Sci 1998, V4, P1 HCAPLUS

IT **176742-08-8**, f 792
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(biol. activity of as oxytocin antagonist)

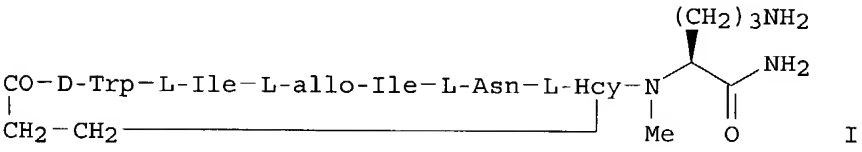
RN 176742-08-8 HCAPLUS

CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



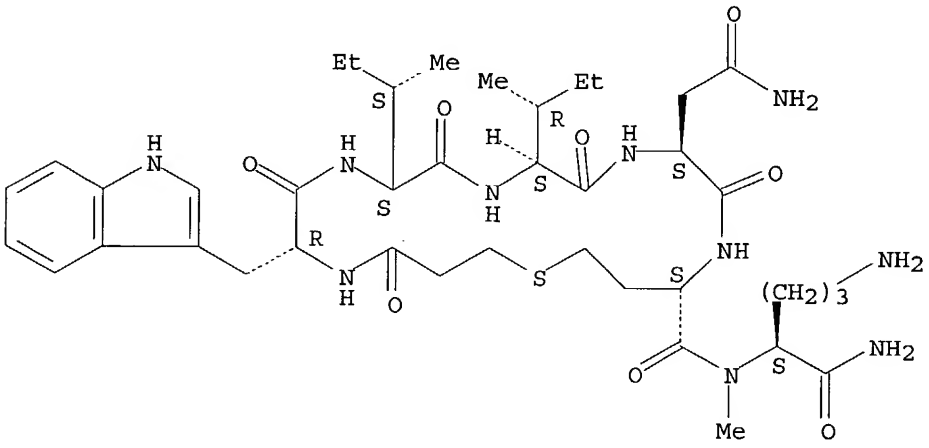
L68 ANSWER 6 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:597870 HCAPLUS
DN 130:14212
ED Entered STN: 22 Sep 1998
TI Synthesis of an oxytocin antagonist - Ferring F 792
AU Nilsson, Anders; Aurell, Carl-Johan; Ekholm, Kjell; Johansson, Erik; Melin, Per; Trojnar, Jerzy; Walhagen, Karin; Wisniewski, Kazimierz
CS Ferring Research Institute AB, Malmo, S-200 61, Swed.
SO Peptides 1996, Proceedings of the European Peptide Symposium, 24th, Edinburgh, Sept. 8-13, 1996 (1998), Meeting Date 1996, 683-684. Editor(s): Ramage, Robert; Epton, Roger. Publisher: Mayflower Scientific, Kingswinford, UK.
CODEN: 66RCA5
DT Conference
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2
GI



AB A symposium report on the solid-phase preparation of the title compound I (Hcy = homocysteine).
ST oxytocin antagonist Ferring F792 solid phase prepn symposium
IT Solid phase synthesis
(peptide; solid-phase preparation of oxytocin antagonist Ferring F792)
IT **176742-08-8P**, F 792
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase preparation of oxytocin antagonist Ferring F792)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Freidinger, R; J Org Chem 1983, V48, P77 HCAPLUS

(2) Melin, P; J Endocrinol 1986, V111, P125 HCAPLUS
(3) Prochazka, Z; Collect Czech Chem Commun 1992, V57, P1335 HCAPLUS
(4) Wade, J; Peptide Research 1991, V4, P194 HCAPLUS
IT **176742-08-8P**, F 792
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase preparation of oxytocin antagonist Ferring F792)
RN 176742-08-8 HCAPLUS
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L68 ANSWER 7 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:388538 HCAPLUS
DN 129:41416
ED Entered STN: 25 Jun 1998
TI Preparation of heptapeptide alcohol oxytocin analogs
IN Melin, Per; Nilsson, Anders; Trojnar, Jerzy; Aurell, Carl-Johan; Riviere, Pierre; Haigh, Robert
PA Ferring B.V., Neth.; Ferring AB
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K007-16
ICS A61K038-11
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 2, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9823636	A1	19980604	WO 1997-SE1968	19971121

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RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

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	AU 9851429	A1	19980622	AU 1998-51429	19971121
	AU 713424	B2	19991202		
	EP 938496	A1	19990901	EP 1997-946210	19971121
	EP 938496	B1	20030604		
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	CN 1129606	B	20031203		
	BR 9713366	A	20000125	BR 1997-13366	19971121
	SI 20026	C	20000229	SI 1997-20076	19971121
	JP 2000507617	T2	20000620	JP 1998-524602	19971121
	JP 3405460	B2	20030512		
	NZ 336445	A	20000623	NZ 1997-336445	19971121
	RU 2180668	C2	20020320	RU 1999-113364	19971121
	HR 970630	B1	20020430	HR 1997-970630	19971121
	EE 3832	B1	20020815	EE 1999-210	19971121
	CA 2272990	C	20021119	CA 1997-2272990	19971121
	AT 242264	E	20030615	AT 1997-946210	19971121
	PT 938496	T	20031031	PT 1997-946210	19971121
	SK 283800	B6	20040203	SK 1999-704	19971121
	ES 2203823	T3	20040416	ES 1997-946210	19971121
	TW 386086	B	20000401	TW 1998-87101258	19980203
	LV 12350	B	19991120	LV 1999-77	19990430
	LT 4650	B	20000425	LT 1999-52	19990511
	NO 9902532	A	19990526	NO 1999-2532	19990526
	US 6143722	A	20001107	US 1999-308912	19990802
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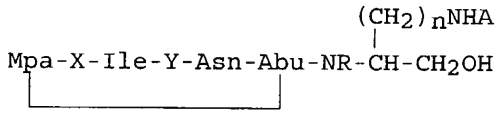
	WO 1997-SE1968	W	19971121		

OS MARPAT 129:41416

GI



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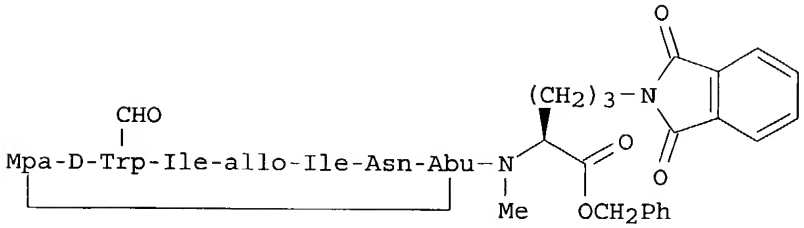


II

AB Heptapeptide alc. oxytocin analogs I [n = 1-6; A = H, C(NH2):NH, R = Me, Et; Mpa = 3-mercaptopropionic acid; Abu = .alpha.-aminobutyric acid; X = D-aromatic .alpha.-amino acid residue; Y = aliphatic .alpha.-amino acid residue]
or pharmaceutically acceptable salts thereof have oxytocin antagonist activity. Also disclosed is: a method of their synthesis; pharmaceutical compns. containing these analogs; the synthesis of such compns.; a method of control of uterine contractions. Thus, protected peptide ester II was

prepared by standard 9-fluorenylmethoxycarbonyl (Fmoc) solid-phase methods, reduced with NaBH4 in aqueous isopropanol, and deprotected with aqueous AcOH at 80.degree. to give desired peptide alc. I (n = 3, A = H, X = D-Trp, Y = allo-Ile). Prepared compds. I showed Ki = 0.1-7.0 nm in an oxytocin receptor assay.

ST oxytocin heptapeptide alc analog prepn; uterine contraction redn oxytocin alc analog

IT Muscle relaxants
(smooth, uterine; preparation of heptapeptide alc. oxytocin analogs)

IT 50-56-6DP, Oxytocin, heptapeptide alc. analogs, preparation
163618-99-3P 176742-08-8P 208400-60-6P
208400-61-7P 208400-62-8P 208400-63-9P
208400-64-0P 208400-65-1P 208400-66-2P
208400-67-3P 208400-68-4P 208400-69-5P
208400-71-9P 208400-73-1P 285571-64-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heptapeptide alc. oxytocin analogs)

IT 208400-74-2P 208400-75-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heptapeptide alc. oxytocin analogs)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Ferring Ab; WO 9200996 A1 1992 HCAPLUS

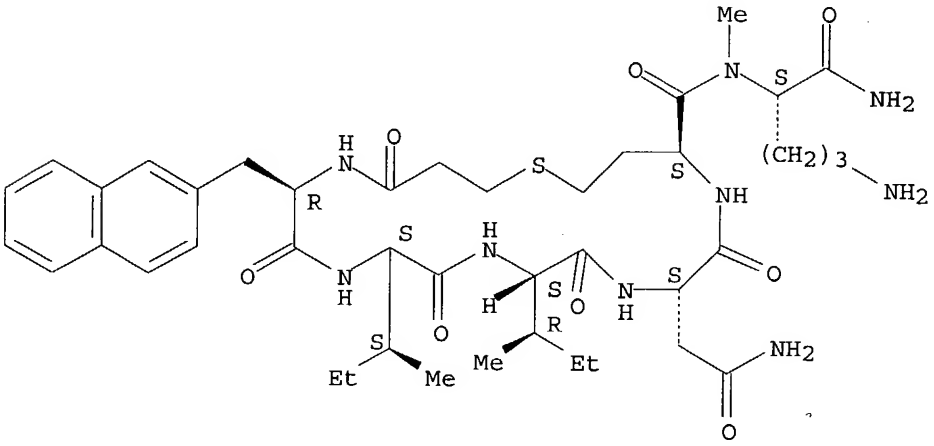
(2) Ferring B V; WO 9502609 A1 1995 HCAPLUS

IT **163618-99-3P 176742-08-8P 208400-60-6P**
208400-61-7P 208400-62-8P 208400-63-9P
208400-64-0P 208400-65-1P 208400-66-2P
208400-67-3P 208400-68-4P 208400-69-5P
208400-71-9P 208400-73-1P 285571-64-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heptapeptide alc. oxytocin analogs)

RN 163618-99-3 HCAPLUS

CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

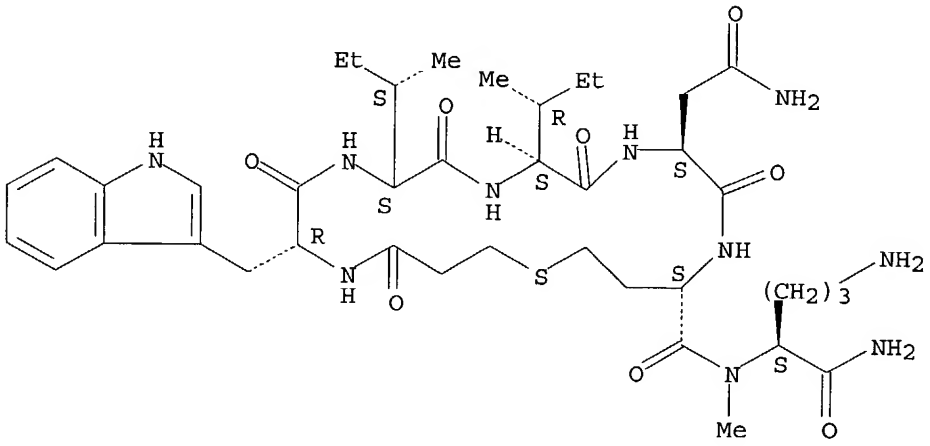
Absolute stereochemistry.



Searched by Noble Jarrell

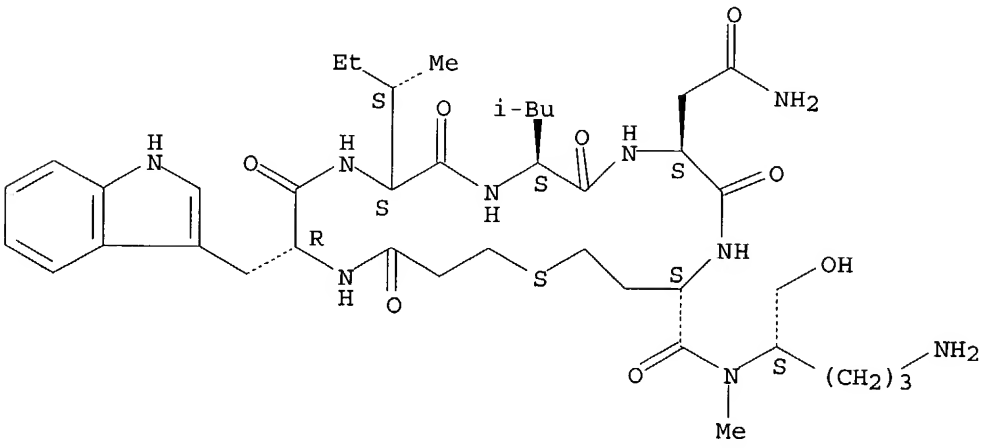
RN 176742-08-8 HCAPLUS
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 208400-60-6 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-leucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

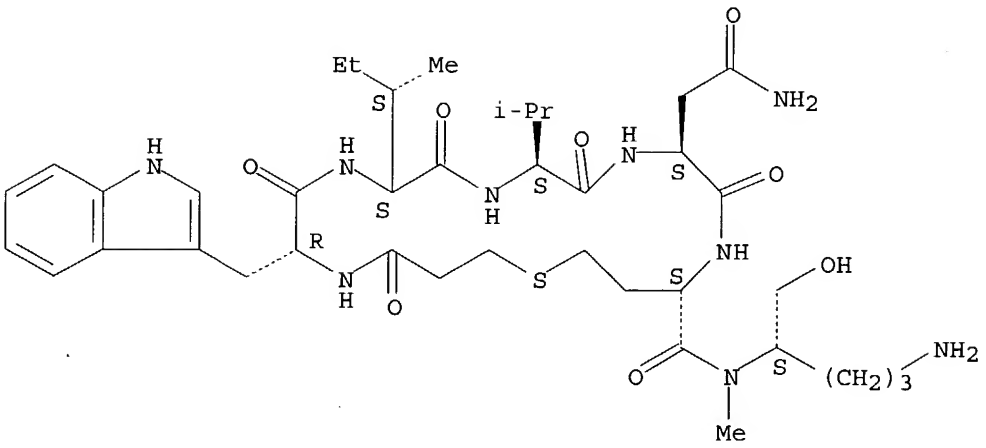
Absolute stereochemistry.



RN 208400-61-7 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-valyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

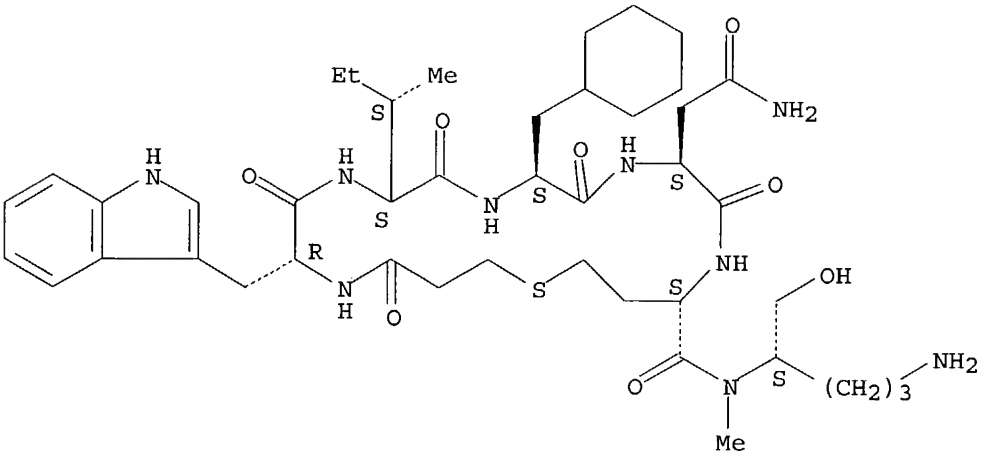
Absolute stereochemistry.

Searched by Noble Jarrell



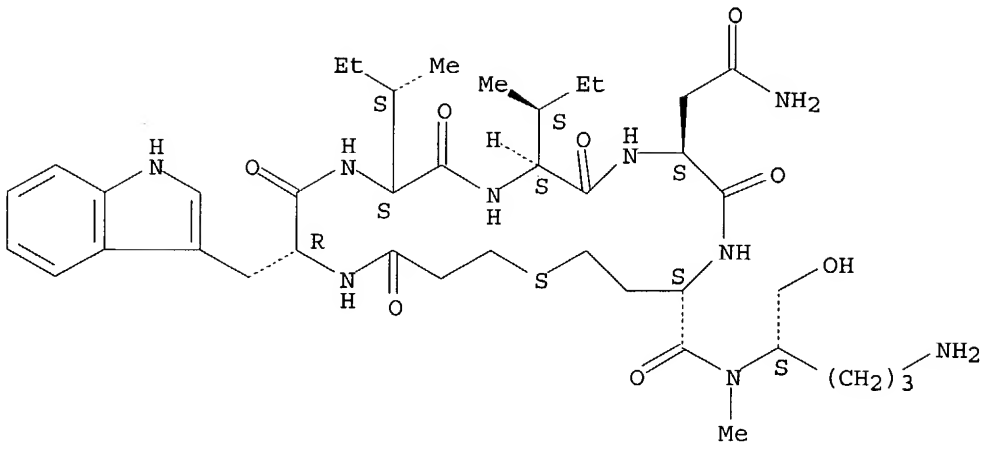
RN 208400-62-8 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-3-cyclohexyl-L-alanyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



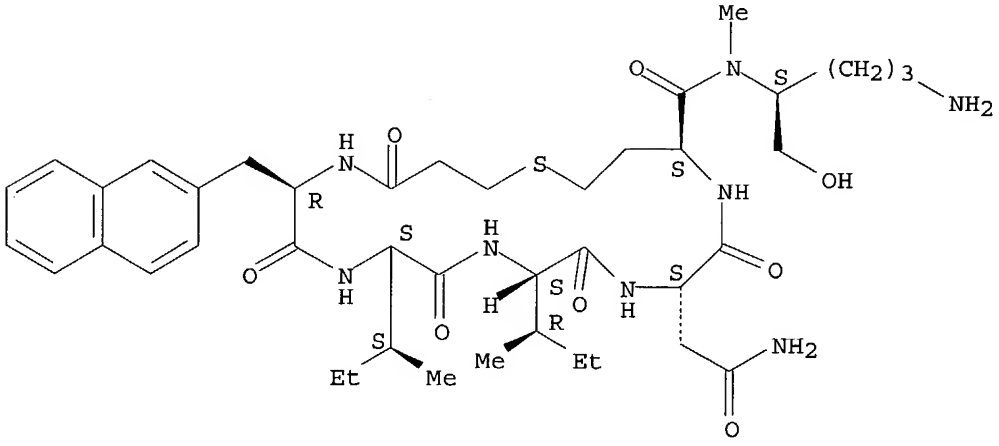
RN 208400-63-9 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-isoleucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



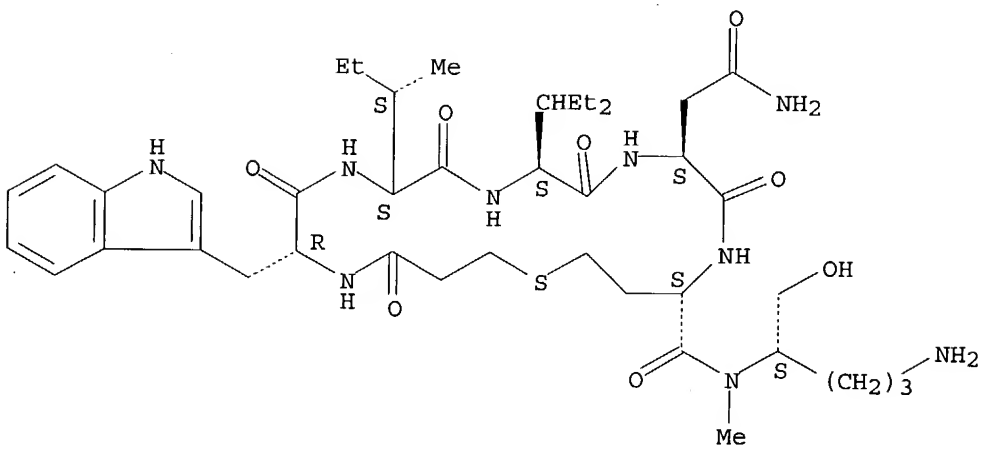
RN 208400-64-0 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



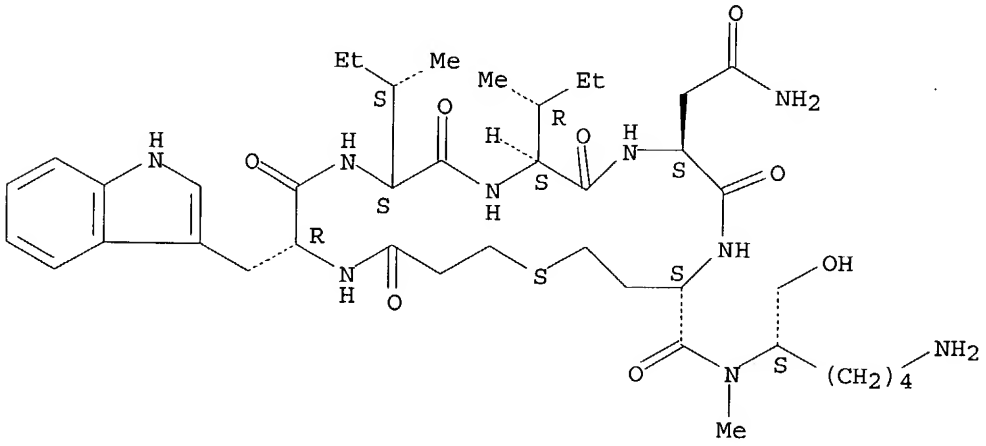
RN 208400-65-1 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-3-ethyl-L-norvalyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



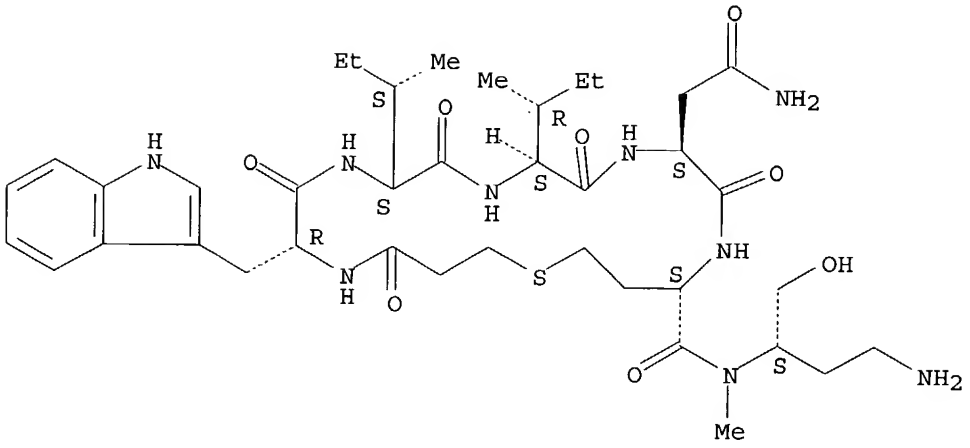
RN 208400-66-2 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-5-amino-1-(hydroxymethyl)pentyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 208400-67-3 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-3-amino-1-(hydroxymethyl)propyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

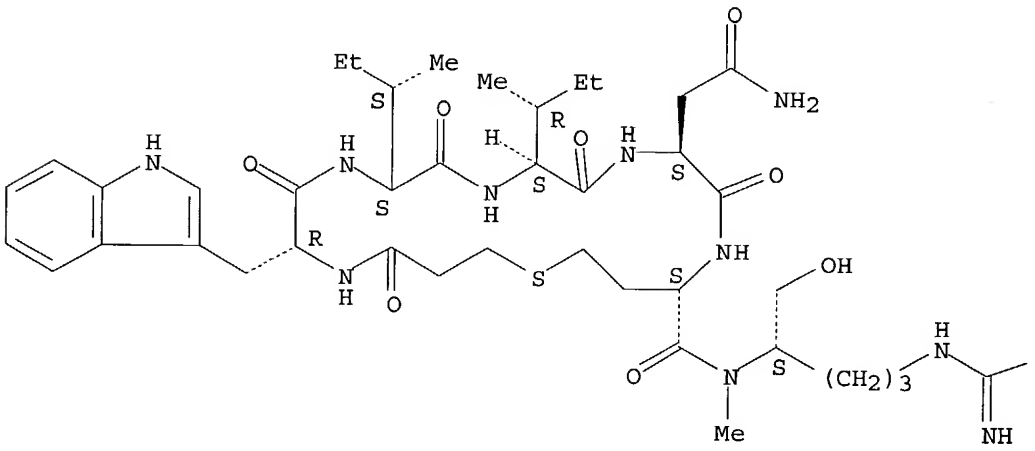
Absolute stereochemistry.



RN 208400-68-4 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-4-[(aminoiminomethyl)amino]-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.

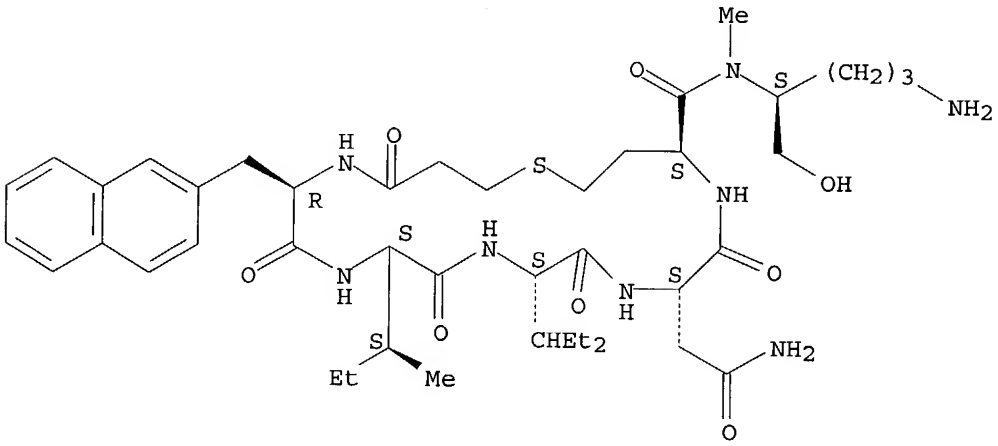
PAGE 1-A



PAGE 1-B

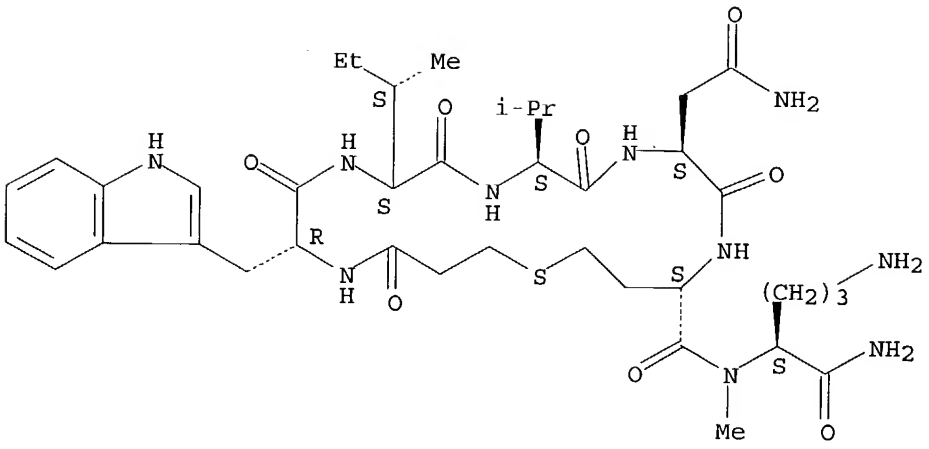
RN 208400-69-5 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-L-isoleucyl-3-ethyl-L-norvalyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



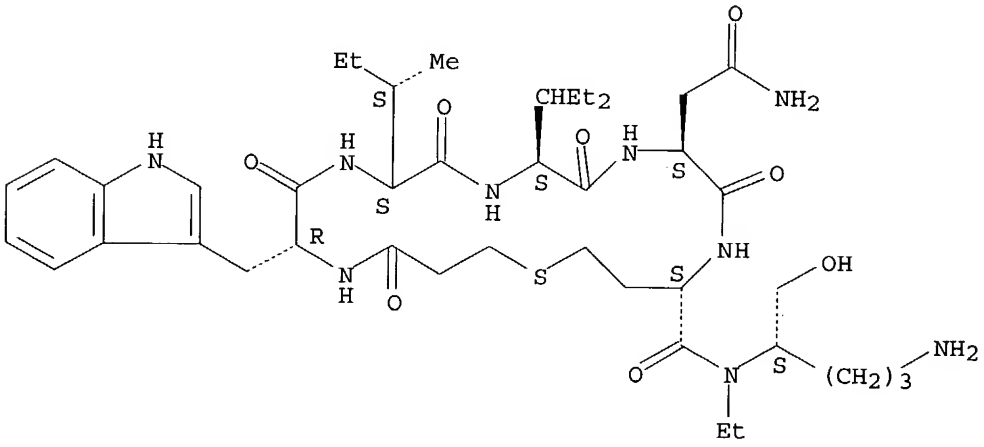
RN 208400-71-9 HCAPLUS
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-valyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



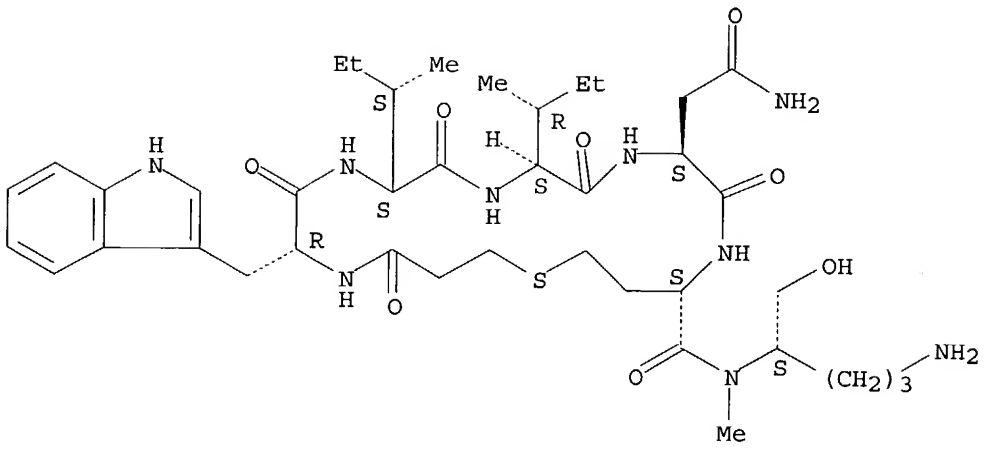
RN 208400-73-1 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-3-ethyl-L-norvalyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-ethyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 285571-64-4 HCAPLUS
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



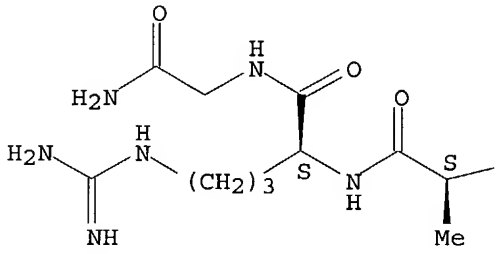
L68 ANSWER 8 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:525203 HCAPLUS
DN 127:156866
ED Entered STN: 16 Aug 1997
TI Fluorescence study of neurohypophyseal hormones and their analogs: distance distributions in a series of arginine-vasopressin analogs
AU Wiczk, W.; Lankiewicz, L.; Kasprzykowski, F.; Oldziej, S.; Szmacinski, H.; Lakowicz, J. R.; Grzonka, Z.
CS Faculty of Chemistry, University of Gdansk, Gdansk, 80-952, Pol.
SO European Biophysics Journal (1997), 26(2), 183-193
CODEN: EBJOE8; ISSN: 0175-7571
PB Springer
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 34
AB Analogs of arginine-vasopressin (AVP) in which substitution of the proline residue in position 7 (by either sarcosine or N-methylalanine) combined with replacement of the cysteine residue in position 1 were the subject of a fluorescence and mol. mechanics study. The authors obtained two groups of analogs: selective antidiuretic agonists (cysteine or .beta.-mercaptopropionic acid in position 1) and pressor and uterotonic antagonists (deamino-penicillamine or .beta.-mercapto-.beta.,.beta.-cyclopentamethylenepropionic acid in position 1). Using frequency-domain measurements of fluorescence resonance energy transfer (FRET) the authors estimated the distance distribution between the phenolic ring of Tyr2 and the disulfide bridge Cys1-Cys6. The authors also analyzed acrylamide quenching of tyrosyl fluorescence to determine the exposure of the tyrosyl ring to the solvent. From fluorescence expts. were compared with those from Monte Carlo simulation (ECEPP/3 force-field).
ST arginine vasopressin analog structure
IT Molecular modeling
(distance distributions in arginine-vasopressin analogs)
IT Conformation
(protein; distance distributions in arginine-vasopressin analogs)
IT 113-79-1D, Arginine vasopressin, analogs 84558-77-0 84558-78-1
84558-81-6 84558-82-7 88463-38-1 88463-39-2
88463-40-5 88463-41-6
RL: PRP (Properties)
(distance distributions in arginine-vasopressin analogs)

IT **84558-81-6 84558-82-7 88463-40-5**
88463-41-6
RL: PRP (Properties)
(distance distributions in arginine-vasopressin analogs)

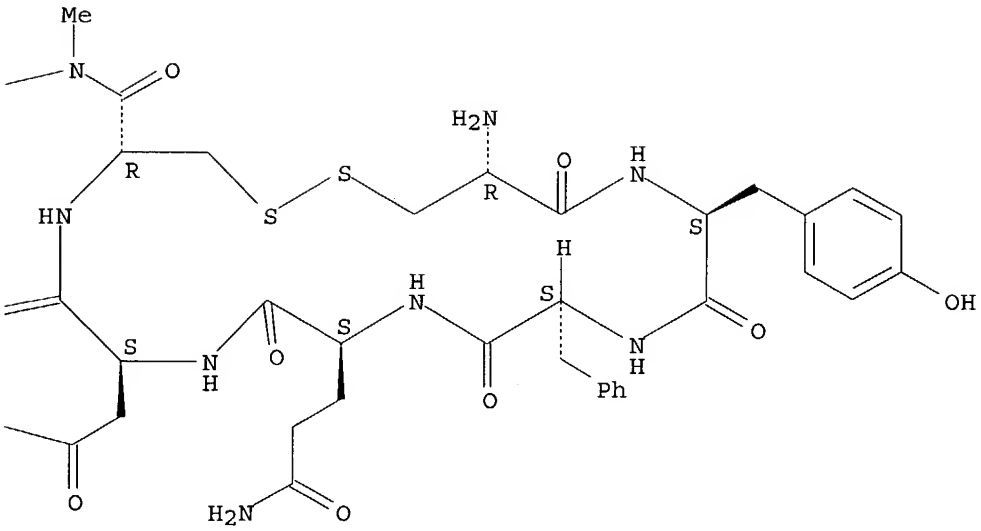
RN 84558-81-6 HCAPLUS
CN Vasopressin, 7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

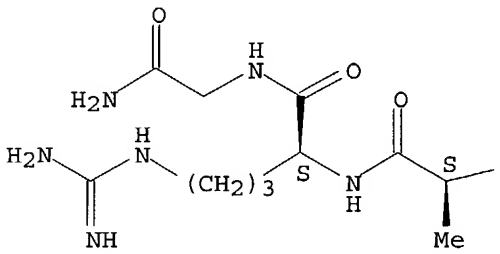


RN 84558-82-7 HCAPLUS

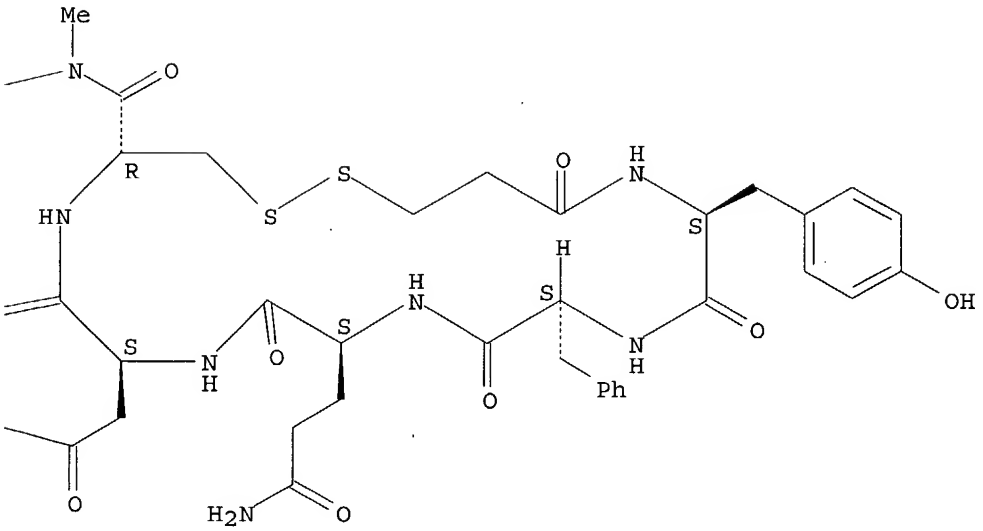
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

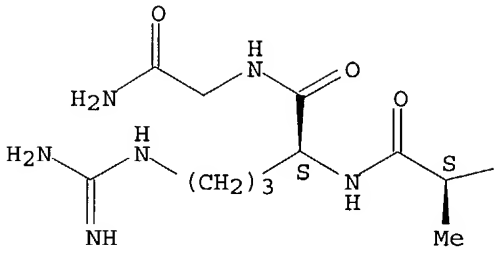


RN 88463-40-5 HCAPLUS
CN Vasopressin, 1-(3-mercapto-3-methylbutanoic acid)-7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

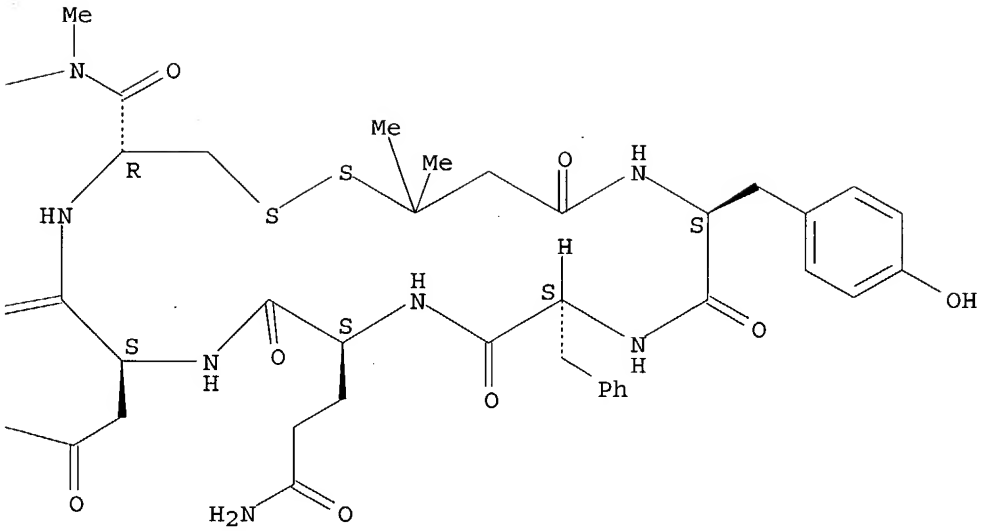
Searched by Noble Jarrell

Absolute stereochemistry.

PAGE 1-A



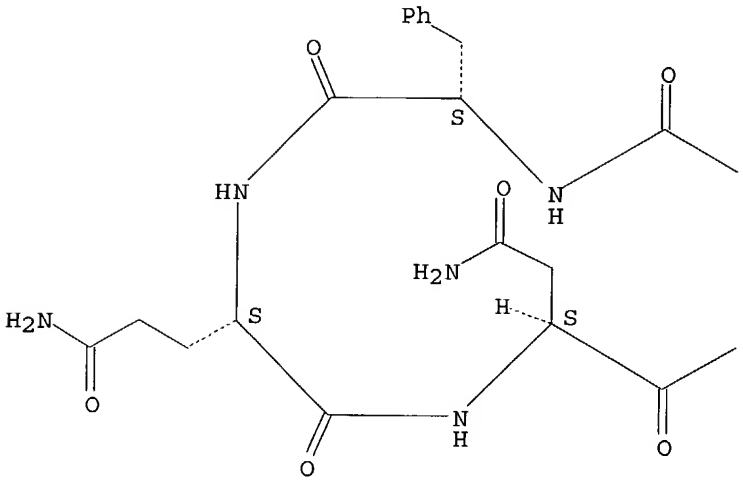
PAGE 1-B



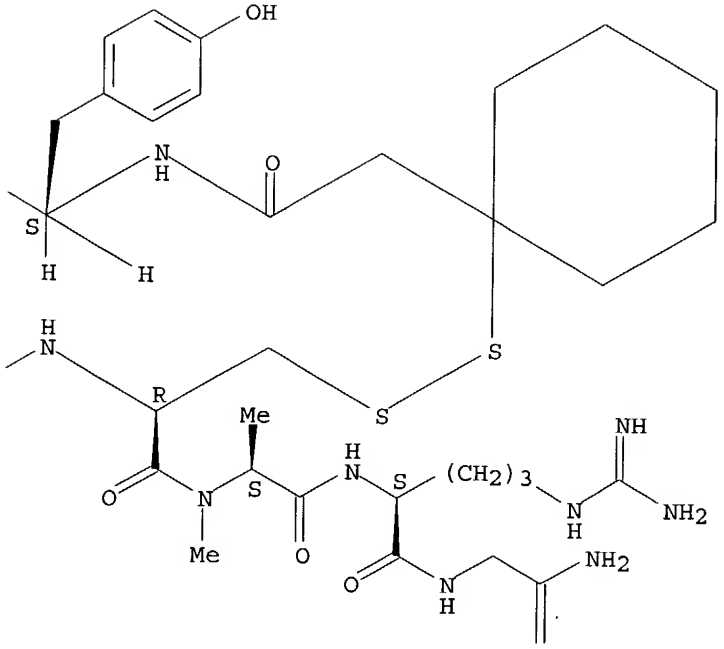
RN 88463-41-6 HCAPLUS
CN Glycinamide, N-[(1-mercaptocyclohexyl)acetyl]-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

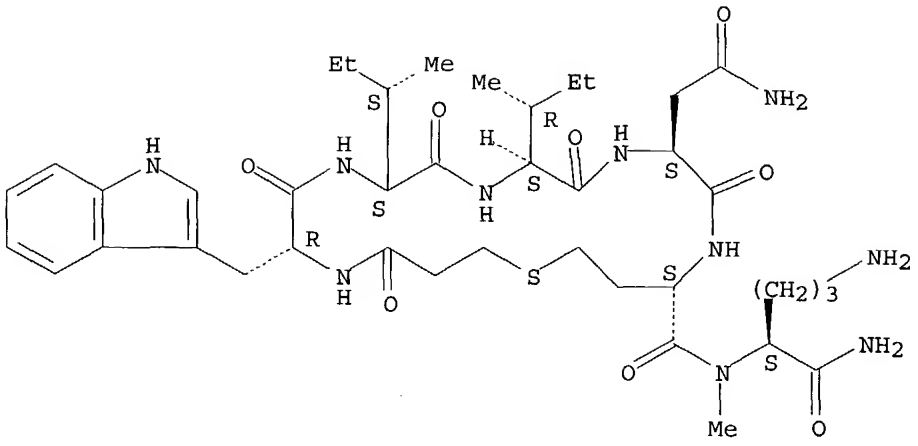


PAGE 2-B

Searched by Noble Jarrell

L68 ANSWER 9 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:277108 HCAPLUS
DN 124:333482
ED Entered STN: 11 May 1996
TI The effect of the oxytocin antagonists F314 and F792 on the in vitro contractility of human myometrium
AU Kinsler, V. A.; Thornton, S.; Ashford, M. L. J.; Melin, P.; Smith, S. K.
CS Rosie Maternity Hospital, University Cambridge, Cambridge, CB2 2SW, UK
SO British Journal of Obstetrics and Gynaecology (1996), 103(4), 373-5
CODEN: BJOGAS; ISSN: 0306-5456
PB Blackwell
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 1
AB In order to investigate whether labor was associated with a change in myometrial response to oxytocin antagonists F314 and F792, the drug effect was examined on spontaneous and oxytocin-induced contractions from myometrium taken either before or after the onset of labor. Results demonstrate that a change in the myometrial response to oxytocin antagonists occurs after the onset of labor. If the antagonists are specific, endogenous oxytocin may be involved in spontaneous activity after the onset of labor. Thus the antagonists should prove to be effective tocolytics.
ST oxytocin antagonist myometrium contractility; tocolytic F314 F792 myometrium contractility
IT Parturition
(oxytocin antagonists F314 and F792 effect on contractility of human myometrium and tocolytic activity)
IT Uterus
(myometrium, oxytocin antagonists F314 and F792 effect on contractility of human myometrium and tocolytic activity)
IT 50-56-6, Oxytocin, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(oxytocin antagonists F314 and F792 effect on contractility of human myometrium and tocolytic activity)
IT 90779-69-4, F 314 **176742-08-8**, F 792
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxytocin antagonists F314 and F792 effect on contractility of human myometrium and tocolytic activity)
IT **176742-08-8**, F 792
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxytocin antagonists F314 and F792 effect on contractility of human myometrium and tocolytic activity)
RN 176742-08-8 HCAPLUS
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L68 ANSWER 10 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:594259 HCAPLUS
DN 123:9933
ED Entered STN: 08 Jun 1995
TI Preparation of peptides exhibiting oxytocin antagonistic activity
IN Aurell, Carl-Johan; Melin, Per; Nilsson, Anders; Trojnar, Jerzy
PA Ferring B. V., Neth.
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K007-16
ICS A61K037-34
ICI C07K099-04
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 1

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PI	WO 9502609	A1	19950126	WO 1994-SE674	19940707
	W: AU, BG, BY, CA, CN, CZ, FI, HU, JP, KR, LT, LV, MD, NO, NZ, PL, RO, RU, SI, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	SE 9302414	A	19950114	SE 1993-2414	19930713
	SE 501678	C2	19950410		
	CA 2163114	AA	19950126	CA 1994-2163114	19940707
	AU 9472406	A1	19950213	AU 1994-72406	19940707
	AU 676071	B2	19970227		
	CN 1126999	A	19960717	CN 1994-192763	19940707
	HU 74874	A2	19970228	HU 1995-3768	19940707
	JP 09502427	T2	19970311	JP 1994-504493	19940707
	EP 791012	A1	19970827	EP 1994-921875	19940707
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	ZA 9405090	A	19950222	ZA 1994-5090	19940713
	NO 9505059	A	19951213	NO 1995-5059	19951213
	FI 9600119	A	19960110	FI 1996-119	19960110
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OS MARPAT 123:9933
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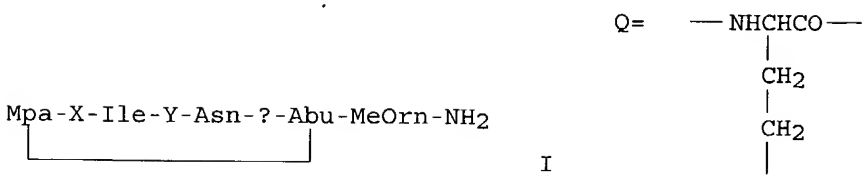


I

AB A peptide having formula [I; Mpa = 3-mercaptopropionic acid residue (SCH2CH2CO); X = D-Trp or .beta.-(2-Naphthyl)-D-alanine (D-Nal); Ile = isoleucine; Y = alloisoleucine (alloIle) or (S)-2-Amino-3-ethyl-pentanoic acid (Ala(.beta.-Et2)); Asn = asparagine; .alpha.-Abu = .alpha.-aminobutyric acid residue (Q); MeOrn = N.alpha.-methylornithine] are prepared The peptide I is used as an active ingredient in a medicament, especially in a pharmaceutical composition for therapeutic treatment of excessive uterus muscle contractions. Thus, I (Y = D-Nal, Y = alloIle), which was synthesized according to Fmoc methodol. on solid phase by using a TentaGel-S-type resin with RAM-linker, showed an I.D. value [I.D. is represented by the antagonist dose which inhibits an agonist dose (2 .times.) to an effect corresponding to the effect of half the agonist dose (.times.)] of 1.8 .+-.0.04 nmol/kg for the oxytocin-induced uterus contraction of Sprague Dawley rats in natural estrus.

ST peptide prepn oxytocin antagonist; mercaptopropionic acid contg peptide; aminobutyric acid contg peptide; uterus muscle contraction inhibition

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (mercaptopropionic acid and .alpha.-aminobutyric acid)-containing peptide sulfides as oxytocin antagonists)

IT Muscle relaxants
Uterus
(preparation of peptides exhibiting oxytocin antagonistic activity for treatment of excessive uterus muscle contractions)

IT 90779-69-4 163619-02-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(oxytocin antagonistic activity)

IT 14328-54-2, N-9-Fluorenylmethoxycarbonyl-(RS)-2-amino-3-ethylpentanoic acid 98441-66-8 132388-59-1 163619-03-2 163619-04-3, Fmoc-D-Trp(Boc)-OH
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling in preparation of peptides exhibiting oxytocin antagonistic activity)

IT 50-56-6, Oxytocin, biological studies
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of (mercaptopropionic acid and .alpha.-aminobutyric acid)-containing peptide sulfides as oxytocin antagonists)

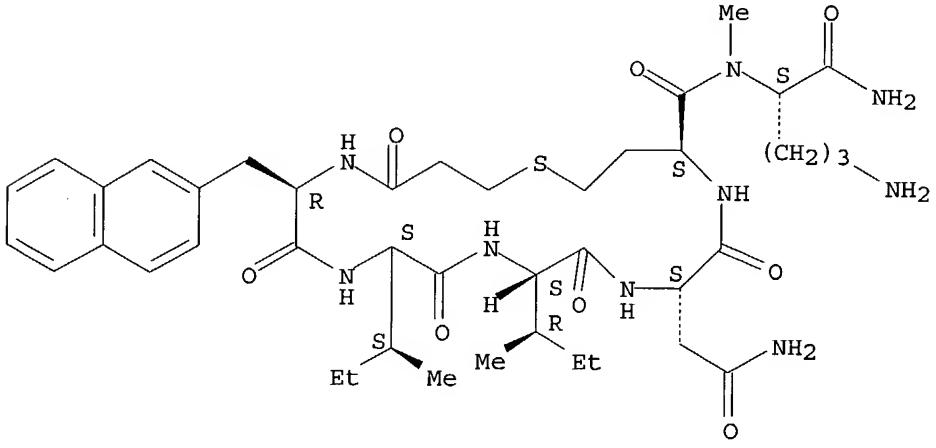
IT **163618-99-3P 163619-00-9P 163619-01-0P 176742-08-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides exhibiting oxytocin antagonistic activity)

IT **163618-99-3P 163619-00-9P 163619-01-0P**

176742-08-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides exhibiting oxytocin antagonistic activity)

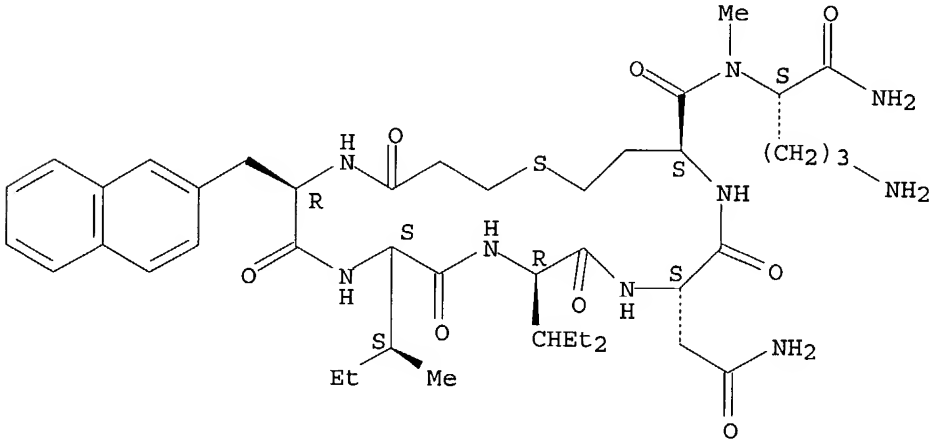
RN 163618-99-3 HCAPLUS
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



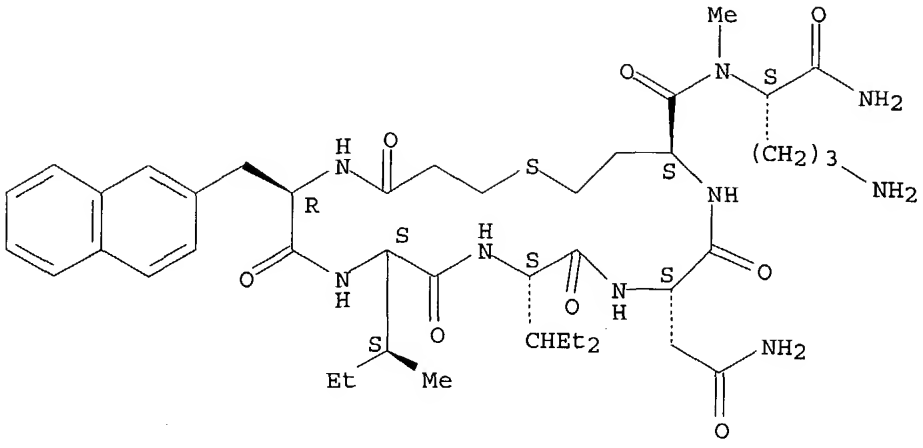
RN 163619-00-9 HCAPLUS
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-L-isoleucyl-3-ethyl-D-norvalyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



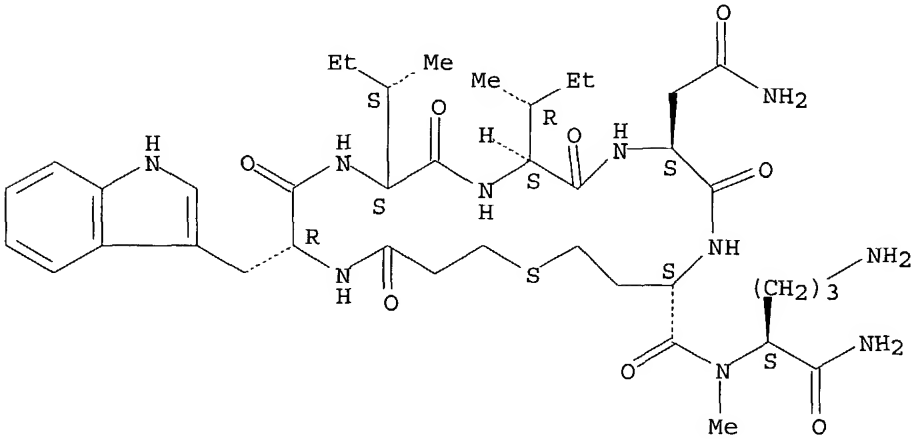
RN 163619-01-0 HCAPLUS
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-L-isoleucyl-3-ethyl-L-norvalyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 176742-08-8 HCAPLUS
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L68 ANSWER 11 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:420658 HCAPLUS
DN 119:20658
ED Entered STN: 24 Jul 1993
TI Antidiuretic activity and release of factor VIII by vasopressin analogs
AU Vilhardt, Hans; Barth, Tomislav; Melin, Per; Aurell, Carl Johan
CS Dep. Med. Physiol., Univ. Copenhagen, Copenhagen, DK-2200, Den.
SO European Journal of Pharmacology (1993), 232(2-3), 223-6
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 1
AB Vasopressin and in particular its structural analog dDAVP

(1-deamino-8-D-arginine vasopressin) can increase plasma concns. of Factor VIII and tissue plasminogen activator (tPA) in some species of animals and in humans. For this reason dDAVP is used therapeutically in the treatment of bleeding episodes in patients suffering from hemophilia A and Von Willebrand's disease. However, the high antidiuretic activity of dDAVP constitutes and unwanted effect in this context. In the present study, a large number of analogs of vasopressin were designed, synthesized and tested in monkeys with the aim of producing compds. in which the Factor VIII-releasing activity was selectively isolated from the vasopressor and antidiuretic actions of the peptides. Apparently, it is possible to sep. these biol. activities; however, none of the analogs tested so far possessed Factor VIII potencies comparable to that of dDAVP.

ST vasopressin analog factor VIII antidiuretic

IT Antidiuretics
Antihypotensives
(vasopressin analogs as, in monkey, antidiuretic activity in relation to)

IT Molecular structure-biological activity relationship
(antidiuretic, of vasopressin analogs)

IT Molecular structure-biological activity relationship
(antihypotensive, of vasopressin analogs)

IT Primate
(nonhuman, antidiuretic activity and release of blood-coagulation factor VIII procoagulant by vasopressin analogs in)

IT 4294-01-3 5591-81-1 7729-65-9 16679-58-6, 1-Deamino-8-D-arginine vasopressin 25255-33-8 38679-65-1 43157-23-9 59385-67-0 59385-68-1 59385-71-6 59599-44-9 65919-02-0 79055-71-3 84558-77-0 85114-98-3 **88463-41-6** 90192-02-2 97906-81-5 97906-82-6 97906-83-7 97906-84-8 110551-37-6 117604-45-2 135247-92-6 135355-69-0 135355-70-3 146556-43-6 146556-44-7 146574-37-0 146574-38-1 147661-45-8 147661-46-9 147661-47-0 147850-97-3 148203-69-4 148203-70-7 148203-71-8 148203-72-9 148203-73-0 148203-74-1 148203-75-2 148203-76-3 148261-30-7 148346-24-1 148346-25-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiuretic activity and blood-coagulation factor VIII procoagulant release by, in monkey, structure in relation to)

IT 113189-02-9, Blood-coagulation factor VIII procoagulant
RL: PROC (Process)
(release of, in marmoset monkey, by vasopressin analogs)

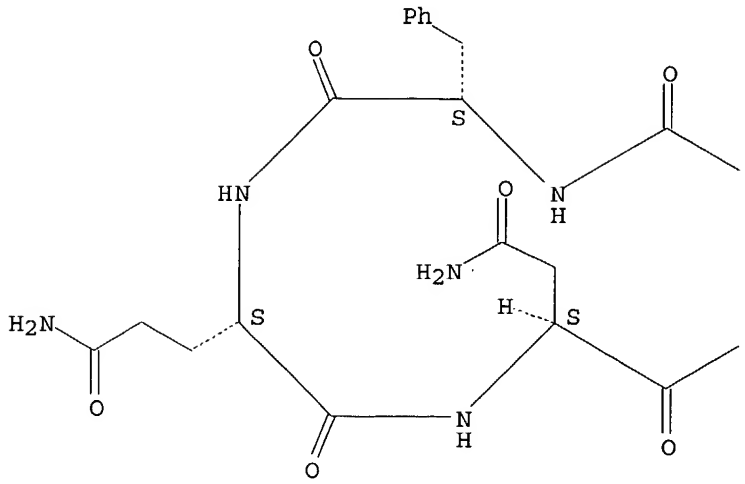
IT **88463-41-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiuretic activity and blood-coagulation factor VIII procoagulant release by, in monkey, structure in relation to)

RN 88463-41-6 HCAPLUS

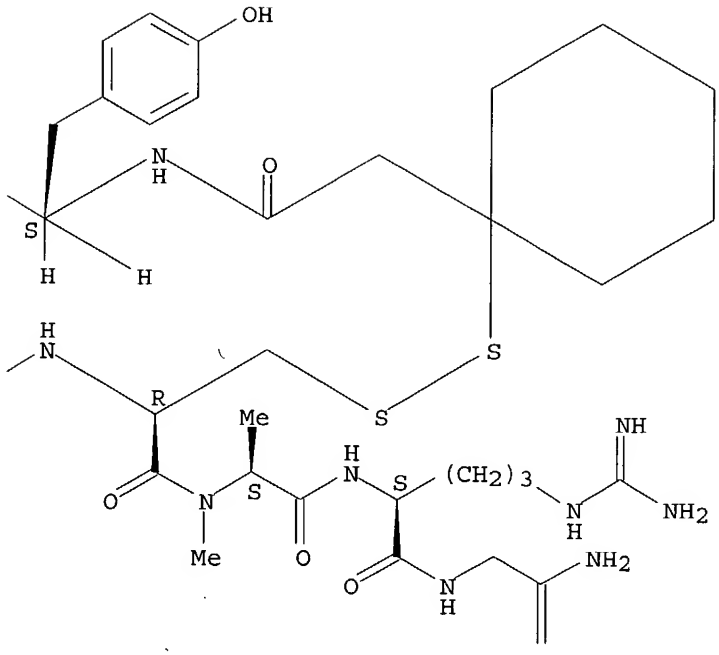
CN Glycinamide, N-[(1-mercaptocyclohexyl)acetyl]-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 2-B

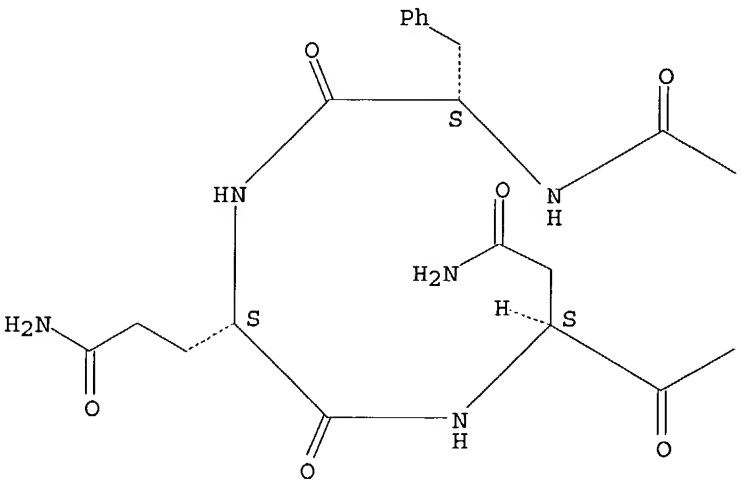
Searched by Noble Jarrell

L68 ANSWER 12 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:152158 HCAPLUS
DN 112:152158
ED Entered STN: 28 Apr 1990
TI Localization of vasopressin binding sites in rat tissues using specific V1 and V2 selective ligands
AU Phillips, Paddy A.; Abrahams, Josephine M.; Kelly, Janice M.; Mooser, Vincent; Trinder, Deborah; Johnston, Colin I.
CS Austin Hosp., Univ. Melbourne, Heidelberg, 3084, Australia
SO Endocrinology (1990), 126(3), 1478-84
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
AB [125I][1-(.beta.-mercapto-.beta.,.beta.-cyclopentamethylene propionic acid), 7-sarcosine] arginine vasopressin ([125I][d(CH2)5,Sarcosine7]AVP), a selective vasopressin V1 antagonist radioligand, bound to regions of the brain, testis, superior cervical ganglion, liver, blood vessels, and renal medulla. Pharmacol. characterization of [125I] [d(CH2)5,Sarcosine7]AVP binding was consistent with that expected for binding to V1 receptors. There was no specific binding demonstrable to pituitary, renal glomeruli, gut, heart, spinal cord, ovary, adrenal medulla, or adrenal cortex. [3H]1-deamino [8-D-arginine] vasopressin ([3H]DDAVP), a potent V2 receptor agonist radioligand, was used to study V2 receptors. Specific binding was only identified in the kidney consistent with the known distribution of antidiuretic V2 receptors on renal collecting tubules. No binding was demonstrated on endothelium or liver where DDAVP might influence clotting factor release, nor in the brain, spinal cord, sympathetic ganglia, heart, or vascular smooth muscle, regions where DDAVP might cause vasodilatation. These studies demonstrate the use of these radioligands to study V1 and V2 receptors in a variety of tissues. Also, since these ligands are selective they are of particular use to study the different receptor subtypes in tissues where V1 and V2 receptors coexist, such as in the kidney.
ST vasopressin receptor subtype ligand; arginine vasopressin analog receptor subtype
IT Receptors
RL: BIOL (Biological study)
(for vasopressin, V1 and V2, specific ligands for)
IT Artery, composition
Blood vessel, composition
Brain, composition
Kidney, composition
Liver, composition
Testis, composition
(vasopressin receptor subtypes of, characterization and localization of)
IT Nerve center and Ganglion
(sympathetic, vasopressin receptor subtypes of, characterization and localization of)
IT **88463-41-6**
RL: BIOL (Biological study)
(as vasopressin receptor V1 ligand)
IT 16679-58-6, DDAVP
RL: BIOL (Biological study)
(as vasopressin receptor V2 ligand)
IT **88463-41-6**
RL: BIOL (Biological study)
(as vasopressin receptor V1 ligand)
RN 88463-41-6 HCAPLUS

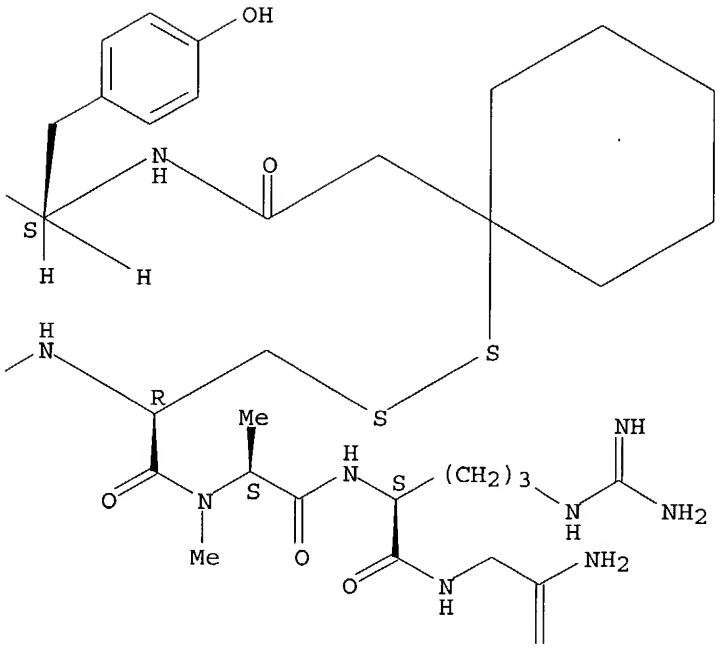
CN Glycinamide, N-[(1-mercaptocyclohexyl)acetyl]-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



Searched by Noble Jarrell

PAGE 2-B

L68 ANSWER 13 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:206154 HCAPLUS
DN 110:206154
ED Entered STN: 10 Jun 1989
TI Vasopressin and oxytocin receptors on plasma membranes from rat mammary gland. Demonstration of vasopressin receptors by stimulation of inositol phosphate formation, and oxytocin receptors by binding of a specific iodine-125 labeled oxytocin antagonist, d(CH2)51[Tyr(Me)2, Thr4, Tyr-NH29]OVT
AU Soloff, Melvyn S.; Fernstrom, Mats A.; Fernstrom, Martha J.
CS Dep. Biochem., Med. Coll. Ohio, Toledo, OH, 43699, USA
SO Biochemistry and Cell Biology (1989), 67(2-3), 152-62
CODEN: BCBIEQ; ISSN: 0829-8211
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
AB The addition of oxytocin to minces of rat mammary gland preincubated with [3H]myo-inositol stimulated the formation of inositol phosphate (IP) in both lactating and regressed glands. Stimulation was .apprx.4 times greater in regressed tissue, consistent with an oxytocin effect on myoepithelial cells, which are enriched relative to epithelial cells during regression. The stimulation of IP formation was agonist specific, as shown with several oxytocin analogs. Arginine vasopressin (AVP), however, was more than twice as potent as oxytocin in stimulating IP formation in regressed tissue. Both V1- and V2-selective AVP receptor antagonists inhibited the stimulation of IP formation by oxytocin. The V1-selective antagonist was .apprx.10 times more inhibitory than the V2-selective antagonist. [3H]AVP was bound to plasma membranes from the mammary gland of the lactating rat with an apparent dissociation constant (Kd) of about 0.7 nM and receptor d. (Bmax) of 54.6 fmol/mg protein. These values were comparable with those found for AVP receptors of kidney plasma membranes. Evidently, the stimulation of IP formation in rat mammary gland by oxytocin occurs through occupancy of AVP, and not oxytocin, receptor sites. Under steady state conditions, [125I]d(CH2)51[Tyr(Me)2,Thr4,Tyr-NH29]OVT [where d(CH2)51 = 1-(.beta.-mercapto-.beta.,.beta.-pentamethylenepropionic acid and OVT = (ornithine8)vasotocin] was bound to a single class of independent binding sites in mammary gland plasma membrane from lactating rats with an apparent Kd of 65 pM and Bmax of 225 fmol/mg protein. Noniodinated antagonist had an affinity .apprx.150 times less than the monoiodinated form. The affinity of binding sites for AVP was 10 times greater than for the noniodinated antagonist and 2.4 times greater than for oxytocin. In view of the presence of AVP receptors in mammary tissue, these findings suggested that the iodinated antagonist binds to AVP receptors. However, comparison of the binding of iodinated antagonist to plasma membranes from the lactating mammary gland with kidney medulla and liver, target sites for AVP, showed that binding was specific for the mammary gland and hence oxytocin receptors. The concentration of oxytocin receptors in mammary gland, as determined by [125I]d(CH2)51[Tyr(Me)2,Thr4,Tyr-NH29]OVT binding, was 4 times greater than the concentration of high-affinity AVP receptors, as determined by [3H]AVP binding. The high affinity, specificity, and specific activity of the iodinated antagonist should make it very useful in further studies to

discriminate between oxytocin and AVP receptors, demonstrate oxytocin receptors with small amts. of samples, perform autoradiog. studies with short-term exposures, and to purify oxytocin receptors.

ST receptor oxytocin vasopressin mammary membrane; inositol phosphate mammary vasopressin receptor

IT Receptors
RL: BIOL (Biological study)
(for oxytocin and vasopressin, of mammary gland membrane, inositol phosphate formation and oxytocin antagonist binding in relation to)

IT Mammary gland
(oxytocin and vasopressin receptors of cell membrane of, inositol phosphate formation and oxytocin antagonist binding in relation to)

IT Lactation
(oxytocin and vasopressin receptors of mammary gland in, inositol phosphate formation and oxytocin antagonist binding in relation to)

IT Cell membrane
(oxytocin and vasopressin receptors of, of mammary gland, inositol phosphate formation and oxytocin antagonist binding in relation to)

IT Cations
(divalent, oxytocin antagonists binding by receptors of mammary gland membrane response to)

IT 27121-73-9, Inositol trisphosphate 27216-57-5, Inositol bisphosphate 105182-27-2, Inositol monophosphate
RL: FORM (Formation, nonpreparative)
(formation of, by mammary gland membrane, oxytocin and vasopressin stimulation of, mechanism for)

IT 2706-70-9 19748-53-9, Glycine-7-oxytocin 77225-24-2, Sarcosine-7-oxytocin **84558-73-6**, N-Methylalanine-7-oxytocin 86969-94-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inositol phosphate formation by mammary gland response to)

IT 7439-96-5, Manganese, biological studies
RL: BIOL (Biological study)
(oxytocin antagonists binding by receptors of mammary gland membrane response to)

IT 114025-20-6 120083-89-8
RL: PROC (Process)
(oxytocin receptor binding of, in mammary gland membrane)

IT 50-56-6, Oxytocin, biological studies
RL: BIOL (Biological study)
(receptors for, of mammary gland membrane, inositol phosphate formation and oxytocin antagonists binding in relation to)

IT 113-79-1, AVP
RL: BIOL (Biological study)
(receptors for, of mammary gland membrane, inositol phosphate formation in relation to)

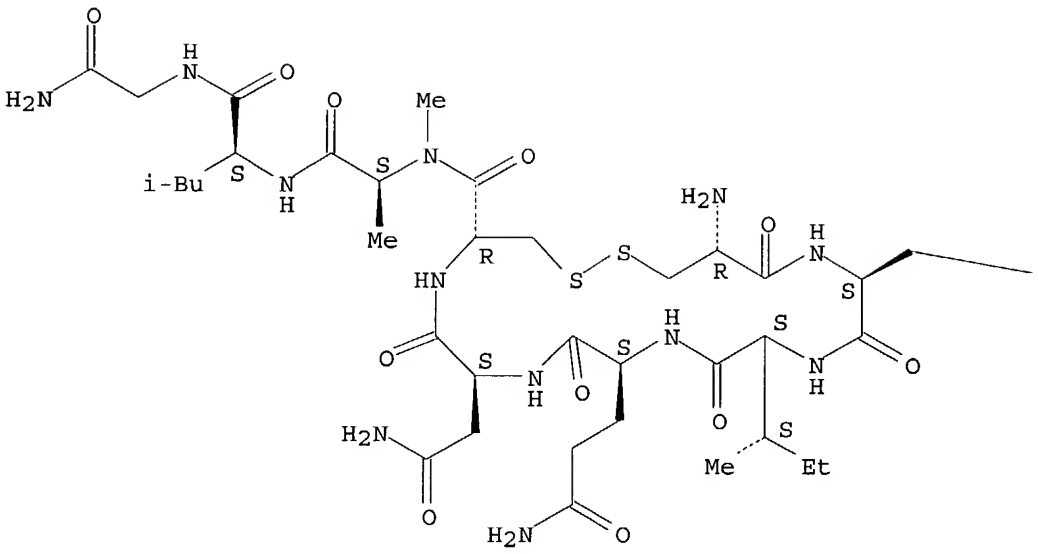
IT **84558-73-6**, N-Methylalanine-7-oxytocin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inositol phosphate formation by mammary gland response to)

RN 84558-73-6 HCAPLUS

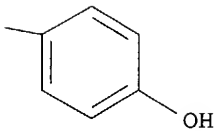
CN Oxytocin, 7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L68 ANSWER 14 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:128055 HCAPLUS
DN 110:128055
ED Entered STN: 15 Apr 1989
TI SKF 105494: a potent antidiuretic hormone antagonist devoid of partial agonist activity in dogs
AU Caldwell, Nancy; Brickson, Bridget; Kinter, Lewis B.; Brooks, David P.; Huffman, William F.; Stassen, Frans L.; Albrightson-Winslow, Christine
CS Dep. Pharmacol., Smith Kline and French Lab., Swedeland, PA, USA
SO Journal of Pharmacology and Experimental Therapeutics (1988), 247(3), 897-901
CODEN: JPETAB; ISSN: 0022-3565
DT Journal
LA English
CC 1-3 (Pharmacology)

AB The purpose of this study was to characterize SKF 104146 and SKF 105494 for water diuretic activity (aquaretic activity) in hydropenic dogs and for antagonism of vasopressin-stimulated antidiuresis in hydrated dogs. The vasopressin receptor affinity and inhibition of vasopressin-stimulated adenylate cyclase activity in renal membranes were also studied. When administered to hydropenic dogs, SKF 101926 (3 or 30 .mu.g/kg) did not cause a water diuresis. Substitution of the dipeptide tail of SKF 101926 with Arg7D-Arg8NH2 (SKF 104146; 30 .mu.g/kg) was associated with a reduction of urine osmolality and an increase in free water clearance. Replacement of the 1 to 6 SS bridge of SKF 104146 with a 1 to 6 dicarba bridge (SKF 105494; 3 .mu.g/kg) was associated with a further reduction of urine osmolality and a net pos. free water clearance. In water-diuretic dogs, SKF 104146 and 105494 shifted the vasopressin dose-response for antidiuresis to the right. SKF 105494 appeared to be 3 times more potent than SKF 104146. In in vitro studies in dog renal plasma membranes, SKF 105494, 104146 and 101926 were potent antagonists of vasopressin stimulation of adenylate cyclase and devoid of detectable agonist activity (up to 10-6M). Thus, in dogs, SKF 105494 is the most potent aquaretic agent identified to date and lacks detectable antidiuretic agonist activity.

ST SKF 105494 diuretic vasopressin receptor structure

IT Receptors
RL: BIOL (Biological study)
(for vasopressin, SKF 105494 and analogs as, diuresis from, structure in relation to)

IT Diuretics
(vasopressin receptor antagonists SKF 105494 and analogs as, structure in relation to)

IT Molecular structure-biological activity relationship
(diuretic, of vasopressin receptor antagonists SKF 105494 and analogs)

IT 90332-82-4 110500-78-2 **110500-82-8** 114923-99-8 119506-31-9 119510-11-1, SKF 105291
RL: BIOL (Biological study)
(diuresis from, vasopressin antagonism in, structure in relation to)

IT 11000-17-2, Vasopressin
RL: BIOL (Biological study)
(receptors for, antagonists of, diuresis from, structure in relation to)

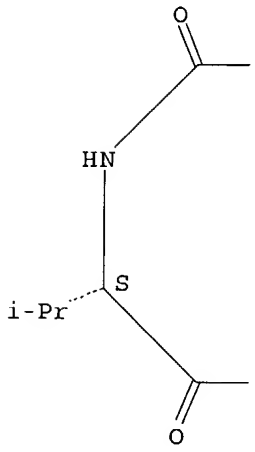
IT **110500-82-8**
RL: BIOL (Biological study)
(diuresis from, vasopressin antagonism in, structure in relation to)

RN 110500-82-8 HCAPLUS

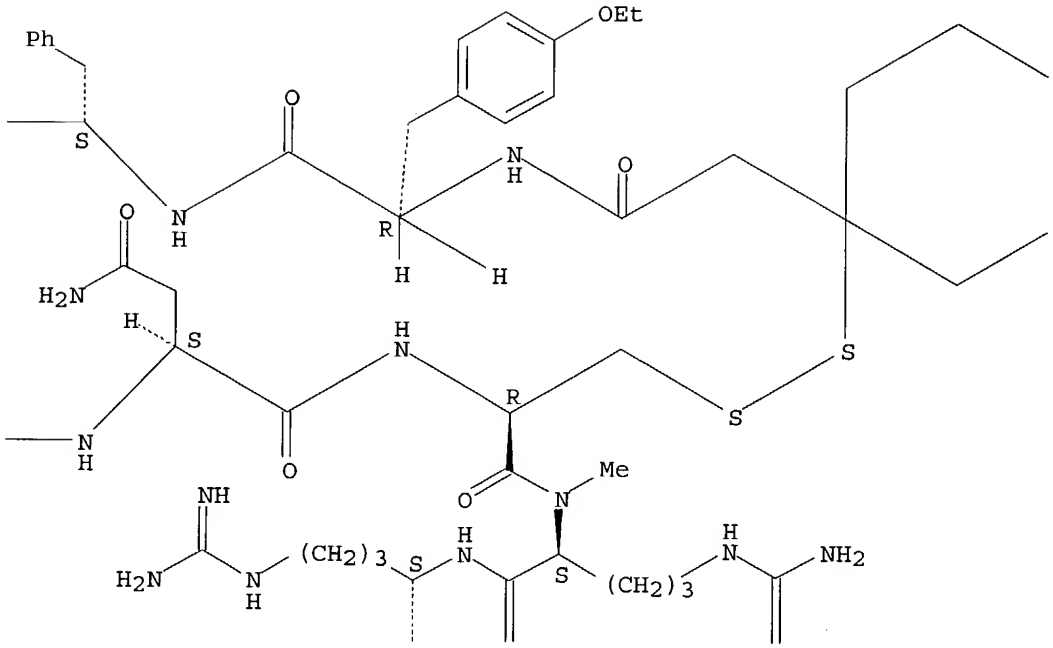
CN L-Argininamide, O-ethyl-N-[(1-mercaptocyclohexyl)acetyl]-D-tyrosyl-L-phenylalanyl-L-valyl-L-asparaginyl-L-cysteinyl-N2-methyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 1-C

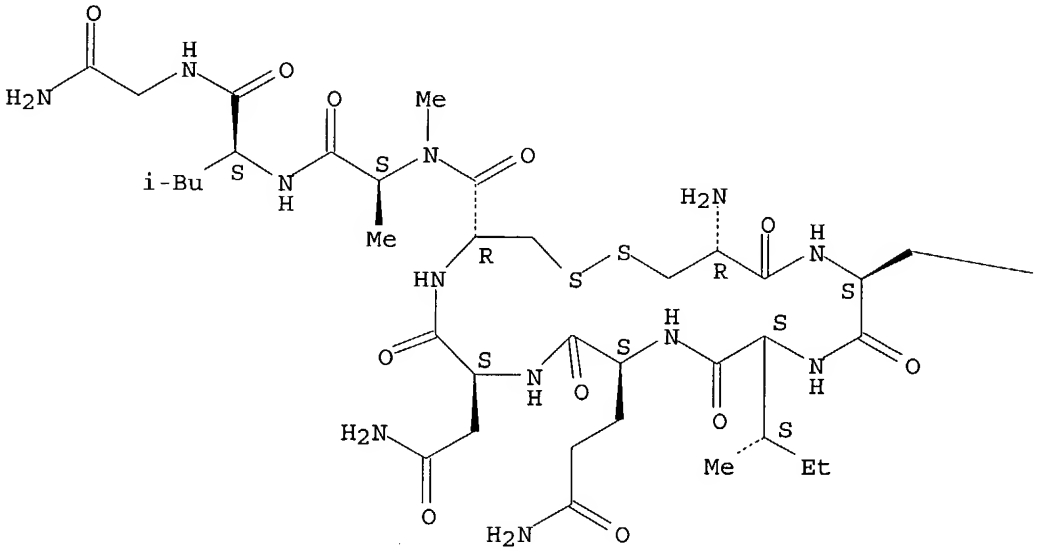
PAGE 2-B

L68 ANSWER 15 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:448726 HCAPLUS
DN 109:48726
ED Entered STN: 19 Aug 1988
TI Identification of a myometrial oxytocin-receptor protein
AU Fahrenholz, Falk; Hackenberg, Mario; Mueller, Michael
CS Max-Planck-Inst. Biophys., Frankfurt, D-6000/70, Fed. Rep. Ger.
SO European Journal of Biochemistry (1988), 174(1), 81-5
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
AB The specific binding of [3H]oxytocin to uterine membrane prepns. derived from different species at late pregnancy was examined The highest receptor d. (bmax value) was found in membranes derived from the myometria of guinea pigs between day 60 post-conception (bmax = 3.6 pmol/mg) and day 65 (bmax = 4.4 pmol/mg). The similarity of dissociation constant (Kd) values for oxytocin binding (Kd = 2.6 nM) and for vasopressin binding (Kd = 2.1 nM) to the same membranes derived from a guinea pig myometrium indicate a homogenous population of high-affinity binding sites which do not discriminate between these 2 hormones. Competitive binding expts. with specific oxytocin agonists containing either sarcosine or N-methylalanine in the place of Pro7 demonstrated that these myometrial receptors have the pharmacol. properties of oxytocin receptors. The analog of 1-deamino-[8-lysine]vasopressin containing a photoreactive azidophenylamidino group at the sidechain of Lys8 retained roughly the same receptor affinity as oxytocin. In photoaffinity labeling expts. with the 3H-labeled analog a membrane protein from guinea pig myometrium with an apparent relative mol. mass (Mr) of 78,000 was preferentially labeled. The labeling of this protein was completely suppressed by a 100-fold molar excess of either oxytocin, or [Sar7]oxytocin, or [Thr4,Sar7]oxytocin, but not by other peptide hormones. These results provide evidence that the labeled 78,000-Mr protein is a myometrial oxytocin-receptor protein.
ST oxytocin receptor protein uterus myometrium
IT Receptors
RL: BIOL (Biological study)
(for oxytocin, of uterus myometrium)

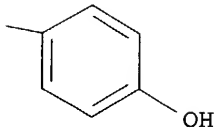
IT Proteins, specific or class
RL: BIOL (Biological study)
(78,000-mol.-weight, oxytocin binding by, of uterus myometrium)
IT Uterus, composition
(myometrium, oxytocin receptor protein of)
IT 50-56-6D, analogs 77225-24-2 84558-69-0 **84558-73-6**
86969-94-0 **86969-96-2** 98791-56-1
RL: BIOL (Biological study)
(oxytocin binding by receptor inhibition by)
IT 113-79-1
RL: BIOL (Biological study)
(oxytocin receptor binding by, in uterus myometrium)
IT 50-56-6, Oxytocin, biological studies
RL: BIOL (Biological study)
(receptors for, of uterus myometrium)
IT **84558-73-6 86969-96-2**
RL: BIOL (Biological study)
(oxytocin binding by receptor inhibition by)
RN 84558-73-6 HCAPLUS
CN Oxytocin, 7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



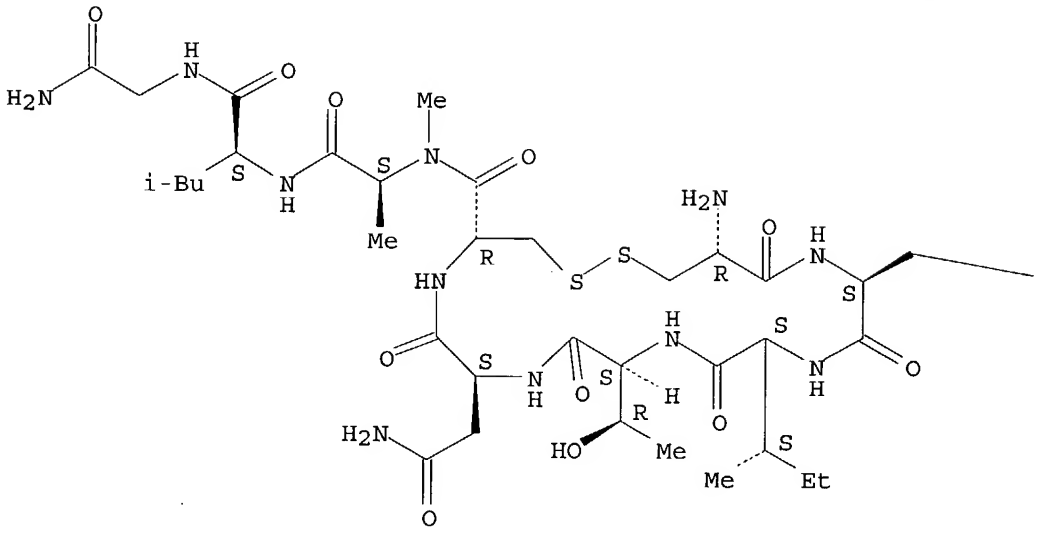
PAGE 1-B



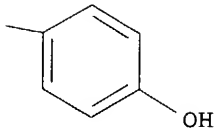
RN 86969-96-2 HCAPLUS
CN Oxytocin, 4-L-threonine-7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



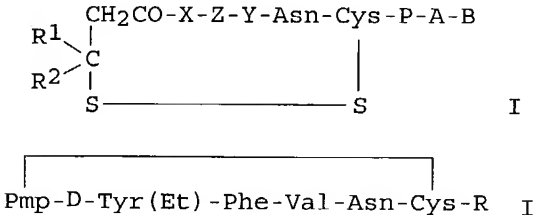
PAGE 1-B



L68 ANSWER 16 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:406980 HCAPLUS
DN 109:6980
ED Entered STN: 09 Jul 1988
TI Preparation of (7-arginine-8-arginine)-vasopressin analogs as vasopressin antagonists
IN Ali, Fadia E.
PA SmithKline Beckman Corp., USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
IC H61K037-34; C07K007-16
NCL 514011000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4717715	A	19880105	US 1986-877571	19860623

PRAI US 1986-877571 19860623
OS MARPAT 109:6980
GI



AB The title peptides [I; P, A = D or L-Arg, Lys, HArg, Me-Arg, Me-Lys, Me-HArg; B = OH, NH2, alkylamino; Z = (4-alkyl)Phe, (O-alkyl)Tyr, Ile; X = D or L-(4-alkyl)Phe, Val, Nva, Leu, Ile, Pba, Nle, Cha, Abu, Met, Chg, (O-alkyl)Tyr; Y = Val, Ile, Abu, Ala, Chg, Gln, Lys, Cha, Thr, Nle, Phe, Leu, Gly; R1, R2 = H, Me; CR1R2 = 4-6 membered cycloalkylene; HArg =

homoarginine; Pba = .alpha.-aminophenylbutyric acid; Cha = cyclohexylalanine; Abu = .alpha.-amino-n-butyric acid; Chg = cyclohexylglycine] were prepared as vasopressin antagonists and diuretics. A vasopressin analog II (Pmp = .beta.-mercapto-.beta.,.beta.-cyclopentamethylenepropionic acid, R = Arg-Arg-NH2) (III) was prepared via the solid-phase method on benzhydrylamine resin. III showed a ED300 (the dose of the compound .mu.g/kg required to lower urine osmolality to 300 mOsm/kg H2O) of 7.2 .mu.g/kg i.p. in an assay for antagonizing antidiuretic hormone using the hydropenic rat screen. A sterile dry powder for parenteral injection containing 0.10 III and 20 mg mannitol is prepared

ST vasopressin analog prepn vasopressin antagonist diuretic

IT Edema
(treatment of, vasopressin analogs for)

IT Diuretics
(vasopressin analogs)

IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(vasopressin analogs, preparation of, as vasopressin antagonists and diuretics)

IT 7536-55-2 13734-34-4 13734-41-3 26340-89-6 87242-91-9 114736-11-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, in preparation of vasopressin antagonist)

IT 61925-77-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and coupling of, to resin, in preparation of vasopressin analog)

IT 13836-37-8DP, resin-bound 61925-77-7DP, resin-bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and peptide coupling with, in preparation of vasopressin antagonist)

IT 110500-89-5DP, resin-bound 110500-91-9DP, benzhydrylamine resin-bound 110500-92-0DP, benzhydrylamine resin-bound 110500-93-1DP, benzhydrylamine resin-bound 110500-94-2DP, resin-bound 110500-95-3DP, benzhydrylamine resin-bound 110517-92-5DP, benzhydrylamine resin-bound 110517-93-6DP, benzhydrylamine resin-bound 114736-12-8DP, benzhydrylamine resin-bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and resin cleavage of, in preparation of vasopressin antagonist)

IT 98612-58-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for vasopressin antagonists)

IT 94497-42-4P 110500-75-9P 110500-76-0P 110500-77-1P 110500-78-2P 110500-79-3P 110500-80-6P 110500-81-7P **110500-82-8P** 110500-84-0P 110517-91-4P 114736-10-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as vasopressin antagonist and diuretic)

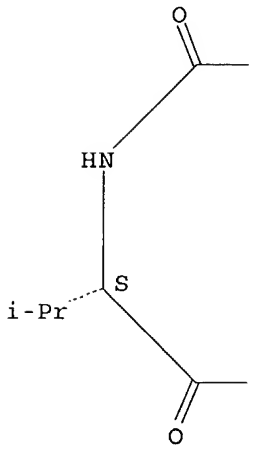
IT **110500-82-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as vasopressin antagonist and diuretic)

RN 110500-82-8 HCAPLUS

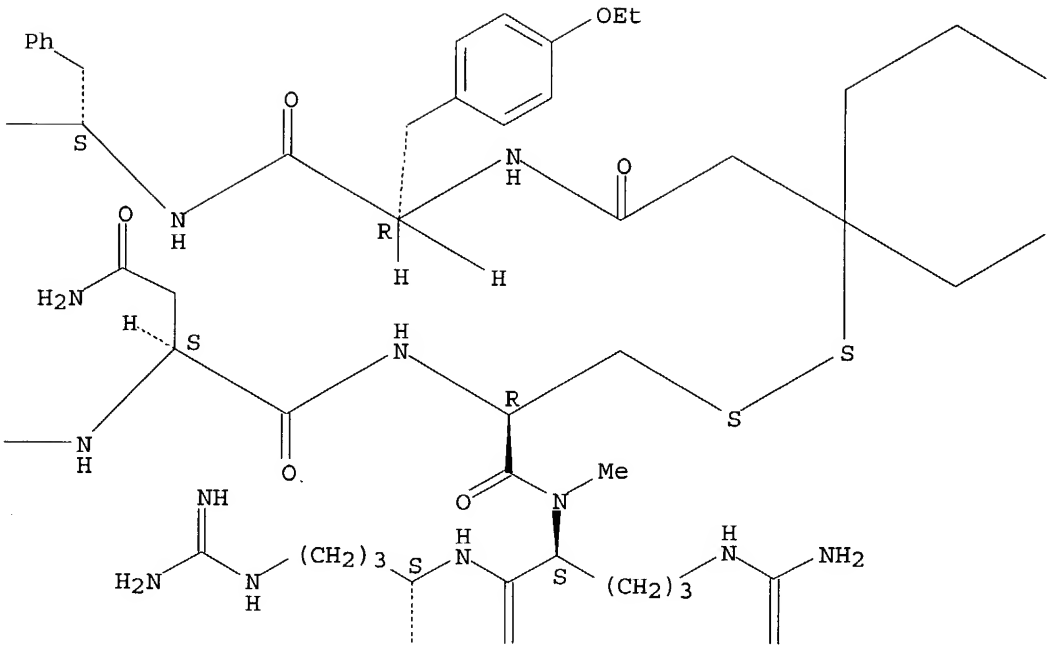
CN L-Argininamide, O-ethyl-N-[(1-mercaptocyclohexyl)acetyl]-D-tyrosyl-L-phenylalanyl-L-valyl-L-asparaginyl-L-cysteinyl-N2-methyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 1-C

PAGE 2-B

L68 ANSWER 17 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:106748 HCAPLUS
DN 108:106748
ED Entered STN: 01 Apr 1988
TI In vivo apparent peptide-receptor dissociation rate constants for arginine vasopressin analogs estimated from inhibition of rat pressor responses
AU Gazis, Diana
CS Mount Sinai Sch. Med., City Univ. New York, New York, NY, 10029, USA
SO Canadian Journal of Physiology and Pharmacology (1987), 65(10), 2099-103
CODEN: CJPPA3; ISSN: 0008-4212
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
AB Apparent pressor receptor dissociation rate consts. for AVP, arginine vasotocin, oxytocin, oxypressin, and [1-deamino-9-D-alanineamide]arginine vasopressin were estimated by the following method. Two minutes after injection of a moderate dose of agonist into urethane-anesthetized rats prepared for recording mean blood pressure, a large dose of inhibitor was injected. Under these conditions, in the 1st few moments after inhibitor injection, there should be no rebinding of the agonist after it dissocs., because vacant receptors should be immediately occupied by inhibitor. The rate of the blood pressure drop at rate consts. thus estimated were 1.1, 1.1, 6.9, 5.8, and 13.9 min-1 for AVP, arginine vasotocin, oxytocin, oxypressin, and [1-deamino-9-D-alanineamide]arginine vasopressin, resp.). These rate consts. were inversely related to the pressor potencies (435, 250, 5, 3, and 0.7 units/mg, resp.) of these 5 compds. Such a relationship is to be expected if decreased potency is in part due to a faster off rate from pressor receptors.
ST vasopressin receptor dissocn rate const; peptide receptor dissocn rate const
IT Kinetics of dissociation
(of vasopressin analog receptor complexes, rate consts. for, blood pressure response in calcn. of)
IT Receptors
RL: BIOL (Biological study)
(vasopressin analog complexes, dissociation of, rate consts. for, blood pressure response in calcn. of)

IT Blood pressure
(vasopressin analogs effect on, peptide-receptor complex dissociation rate consts. calcn. from)

IT 50-56-6D, Oxytocin, receptor complexes 113-79-1D, Arginine vasopressin, receptor complexes 113-80-4D, Arginine vasotocin, receptor complexes 642-35-3D, Oxypressin, receptor complexes 78338-40-6D, receptor complexes
RL: BIOL (Biological study)
(dissociation of, rate constant for, blood pressure response in calcn. of)

IT 111203-41-9D, receptor complexes 111203-42-0D, receptor complexes **111203-43-1D**, receptor complexes 113096-92-7D, receptor complexes
RL: BIOL (Biological study)
(dissociation of, rate consts. for, vasopressin inhibitor potency in relation to)

IT 11000-17-2D, Vasopressin, analogs
RL: BIOL (Biological study)
(receptor dissociation rate consts. for, blood pressure response in calcn. of)

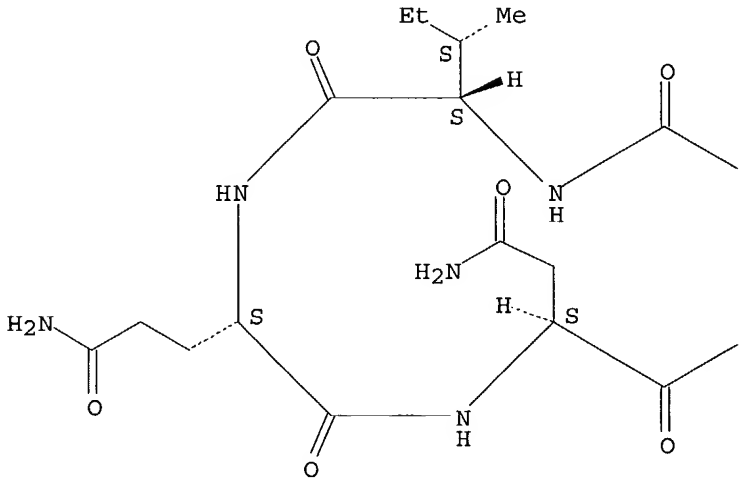
IT **111203-43-1D**, receptor complexes
RL: BIOL (Biological study)
(dissociation of, rate consts. for, vasopressin inhibitor potency in relation to)

RN 111203-43-1 HCAPLUS

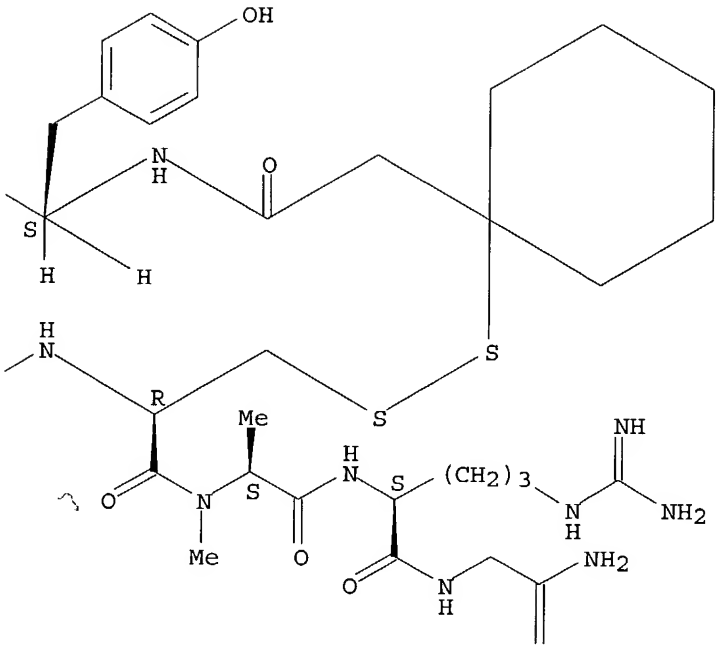
CN Glycinamide, N-[(1-mercaptocyclohexyl)acetyl]-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 2-B

L68 ANSWER 18 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:568932 HCAPLUS
DN 107:168932
ED Entered STN: 14 Nov 1987
TI Further synthetic studies on position 1 of angiotensin II
AU Cordopatis, P.; Theodoropoulos, D.
CS Dep. Chem., Univ. Patras, Patras, 26200, Greece
SO Pept., Proc. Eur. Pept. Symp., 19th (1987), Meeting Date 1986, 633-6. Editor(s): Theodoropoulos, Dimitrios. Publisher: de Gruyter, Berlin, Fed. Rep. Ger.
CODEN: 56ABA8
DT Conference
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 34
AB [7-(trans-4-Hydroxy)-L-proline] arginine vasopressin, [1-desamino,7-(trans-4-hydroxy)-L-proline] arginine vasopressin, and [1-desamino,7-(cis-4-hydroxy)-L-proline) arginine vasopressin were synthesized and their biol. activities were evaluated. Introduction of a hydroxy group on proline enhanced the antidiuretic and uterine activities, but depressed pressor activity. The cis-enantiomer was somewhat less active than the trans-enantiomer, but it was still very active. Deamination increased the diuretic activity. All 7-substituted analogs had antidiuretic activity, but those with some electronegativity on the proline ring (hydroxyproline

or dehydroproline) were extremely active. For pressor activity, the critical requirement was an intact proline ring with no added bulk. Uterine activity was greatest in the hydroxyproline analogs, which have strikingly higher activities than vasopressin.

ST vasopressin analog structure activity; antidiuresis vasopressin analog; uterus contraction vasopressin analog; blood pressure vasopressin analog

IT Uterus
(contraction of, vasopressin 7-hydroxyproline-substituted analogs effect on, structure in relation to)

IT Antidiuretics
(vasopressin 7-hydroxyproline-substituted analogs as)

IT Blood pressure
(vasopressin 7-hydroxyproline-substituted analogs effect on, structure in relation to)

IT Molecular structure-biological activity relationship
(antidiuretic, of vasopressin 7-hydroxyproline-substituted analogs)

IT Molecular structure-biological activity relationship
(blood pressure-affecting, of vasopressin 7-hydroxyproline-substituted analogs)

IT Molecular structure-biological activity relationship
(uterus contraction-affecting, of vasopressin 7-hydroxyproline-substituted analogs)

IT 113-79-1 113-81-5 47915-22-0 66185-31-7 66185-32-8 84558-77-0 84558-78-1 **84558-81-6 84558-82-7**
RL: PRP (Properties)
(activity of, structure in relation to)

IT 113-79-1DP, Arginine vasopressin, 7-hydroxyproline-substituted analogs 108666-16-6P 108666-17-7P 110849-45-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and bioactivity of, structure in relation to)

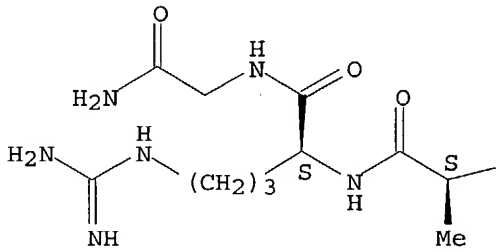
IT **84558-81-6 84558-82-7**
RL: PRP (Properties)
(activity of, structure in relation to)

RN 84558-81-6 HCAPLUS

CN Vasopressin, 7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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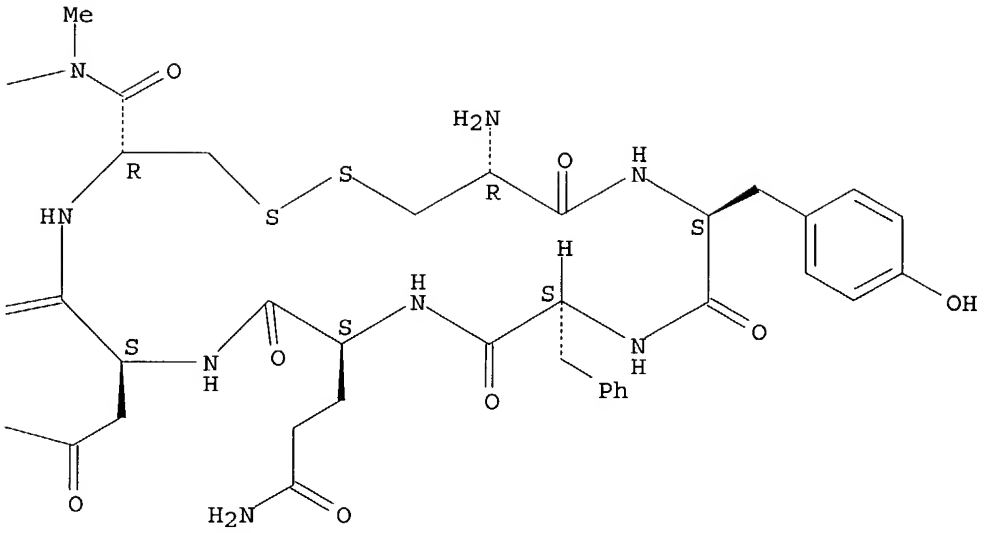
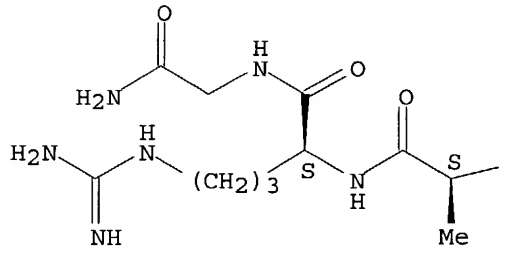


RN 84558-82-7 HCAPLUS
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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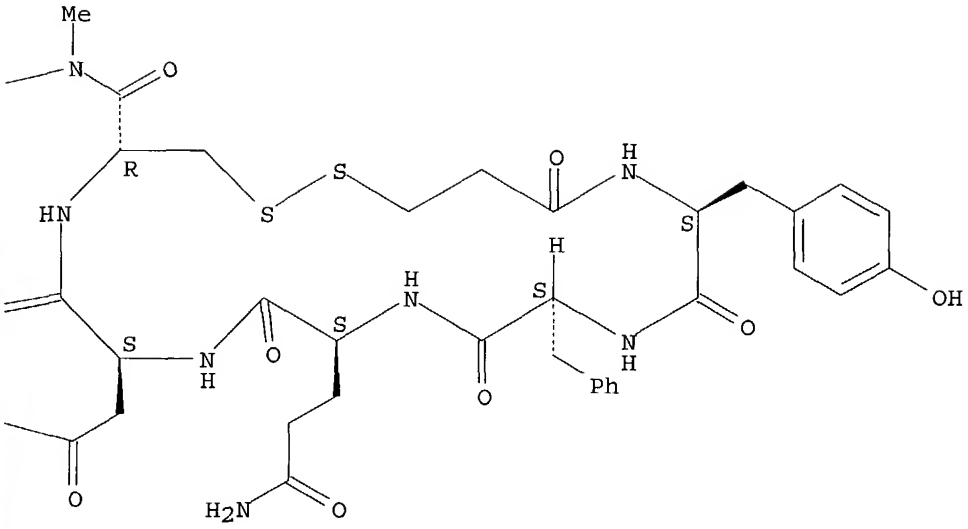

L68 ANSWER 19 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:554755 HCAPLUS
DN 107:154755
ED Entered STN: 31 Oct 1987
TI Vasopressin antagonists
IN Fadia, Elfehail Ali
PA SmithKline Beckman Corp., USA
SO Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07K007-06
ICS C07K007-16; A61K037-02
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 206730	A2	19861230	EP 1986-304652	19860617
	EP 206730	A3	19881102		
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	AU 8658384	A1	19861224	AU 1986-58384	19860605
	AU 595201	B2	19900329		
	ZA 8604242	A	19870429	ZA 1986-4242	19860606
	FI 8602572	A	19861219	FI 1986-2572	19860617
	NO 8602406	A	19861219	NO 1986-2406	19860617
	ES 556141	A1	19870816	ES 1986-556141	19860617
	CN 86104835	A	19861217	CN 1986-104835	19860618
	DK 8602858	A	19861219	DK 1986-2858	19860618
	JP 61293999	A2	19861224	JP 1986-143975	19860618
	HU 41051	A2	19870330	HU 1986-2567	19860618
PRAI	US 1985-747640		19850618		

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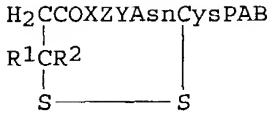

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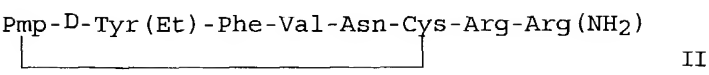


II

AB The cyclic peptides I [A, P = D- or L- Arg, Lys, HArg, MeArg, MeLys, or MeHArg (HArg = homoarginine, MeArg = N-methylarginine); B = OH, NH2, NHalk (alk = C1-4 alkyl); Z = Phe, Phe(4'-alk), Tyr(alk), Ile, or Tyr; X = D- or L-Phe, Phe(4'-alk), Val, Nva, Leu, Ile, Tyr, Pba, Nle, Cha, Abu, Met, Chg, Tyr, Tyr(alk) (Pba = a-aminophenylbutyric acid, Nle = norleucine, Cha = cyclohexylalanine, Abu = .alpha.-aminobutyric acid, Chg = cyclohexylglycine); Y = Val, Ile, Abu, Ala, Chg, Gln, Lys, Cha, Nle, Thr, Phe, Leu, Gly; R1, R2 = H, Me; CR1R2 = C4-6 cycloalkylene] are prepared as vasopressin antagonists. Thus, the protected peptide intermediate resin Pmp (4-MeBzl)-D-Tyr(Et)-Phe-Val-Asn-Cys(4-MeBzl)-Arg(Tos)-Arg(Tos)-BHA [Pmp = 1-(.beta.-mercapto-B,B-cyclopentamethylene)propionic acid; BHA = benzhydrylamine resin] was prepared by solid-state methods, using tert-butyloxycarbonyl for protection. The peptide was cleaved from the resin with deprotection, using anisole-containing anhydrous HF, at 0.degree.. The peptide was oxidatively cyclized with K3[Fe(CN)6] at pH 7.2, followed by pH adjustment to 4.5 (HOAc) and passage through a weakly acid acrylic resin column (Bio-Rex 70). Elution with pyridine-HOAc-H2O (30:4:66) gave II. II (7.2 .mu.g/kg), administered i.p., had antidiuretic activity, as shown in the hydropenic rat model. I can be used as antihypertensive, antioxytocic and diuretic drug.

ST cyclic octapeptide prepn vasopressin antagonist

IT Antihypertensives
Diuretics
(cyclic octapeptides)

IT 50-56-6, Oxytocin, biological studies
RL: BIOL (Biological study)
(antagonists of, cyclic octapeptides as)

IT 11000-17-2P, Vasopressin
RL: SPN (Synthetic preparation); PREP (Preparation)
(antagonists, cyclicoctapeptides, preparation of)

IT 110500-89-5DP, resin-bond
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and deprotection-cleavage of)

IT 110500-88-4P 110500-90-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidative cyclization of)

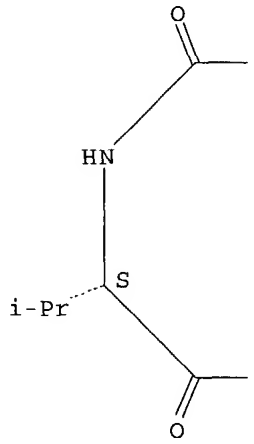
IT 110500-91-9DP, benzhydrylamine resin-bound 110500-92-0DP, benzhydrylamine resin-bound 110500-93-1P 110500-95-3P 110517-92-5DP, benzhydrylamine resin-bound 110517-93-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and resin cleavage-deblocking of)

IT 110500-94-2DP, choromethylated Ph resin-bound 110500-96-4DP, choromethylated Ph resin-bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 94497-42-4P 98612-58-9P 110500-75-9P 110500-76-0P 110500-77-1P
110500-78-2P 110500-79-3P 110500-80-6P 110500-81-7P
110500-82-8P 110500-83-9P 110500-84-0P **110500-85-1P**
110517-91-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as vasopressin antagonist)
IT 61315-61-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase peptide coupling of)
IT 13836-37-8 76757-92-1 108695-16-5 110500-86-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase peptide coupling of, in preparation of vasopressin antagonist)
IT 7536-55-2 13734-34-4 13734-41-3 54613-99-9 61925-77-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase peptide coupling with, in preparation of vasopressin antagonist)
IT 100304-73-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase peptide synthesis with)
IT 13836-37-8D, resin-bond 93449-74-2D, benzhydrylamine resin-bound
110500-87-3D, Benzhydrylamine resin-bound
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase peptide synthesis with, in preparation of vasopressin antagonist)
IT **110500-82-8P 110500-85-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as vasopressin antagonist)
RN 110500-82-8 HCAPLUS
CN L-Argininamide, O-ethyl-N-[(1-mercaptocyclohexyl)acetyl]-D-tyrosyl-L-phenylalanyl-L-valyl-L-asparaginyl-L-cysteinyl-N2-methyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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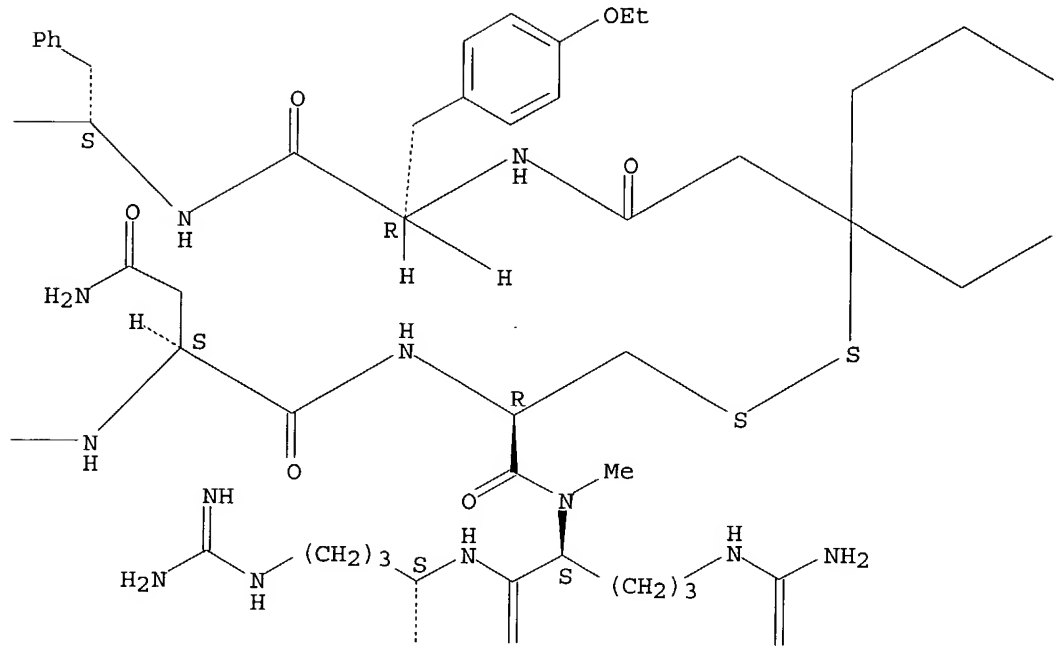
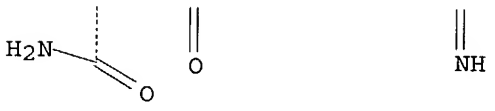


PAGE 1-C

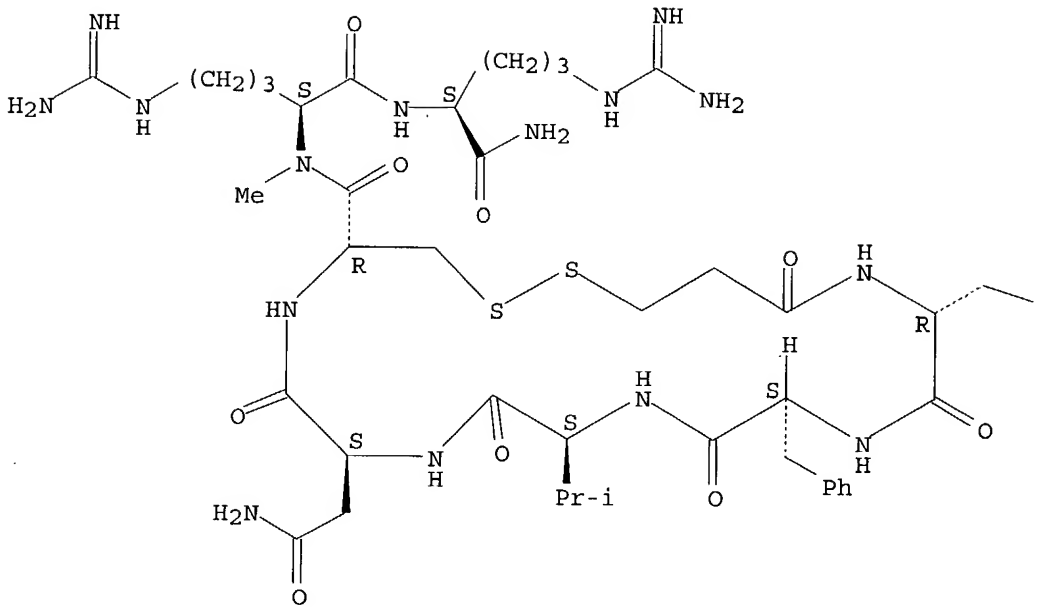
PAGE 2-B



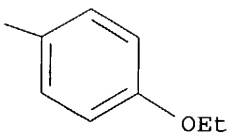
RN 110500-85-1 HCAPLUS
CN L-Argininamide, O-ethyl-N-(3-mercapto-1-oxopropyl)-D-tyrosyl-L-phenylalanyl-L-valyl-L-asparaginyl-L-cysteinyl-N2-methyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L68 ANSWER 20 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:27885 HCAPLUS
DN 106:27885
ED Entered STN: 07 Feb 1987
TI Interaction of rat adenohypophyseal vasopressin receptors with vasopressin analogs substituted at positions 7 and 1: dissimilarity from the V1 vasopressin receptor
AU Knepel, Willhart; Goetz, Doris; Fahrenholz, Falk
CS Dep. Pharmacol., Univ. Freiburg, Freiburg/Br., Fed. Rep. Ger.
SO Neuroendocrinology (1986), 44(3), 390-6
CODEN: NUNDAJ; ISSN: 0028-3835
DT Journal

LA English
CC 2-2 (Mammalian Hormones)
AB Vasopressin [11000-17-2] analogs substituted in positions 7 and 1 were used to determine whether or not rat adenohypophyseal vasopressin receptors have a ligand selectivity which is similar to that of the V1 subtype of vasopressin receptors. By incubating rat anterior pituitary quarters or by perifusing rat isolated anterior pituitary cells, the effect of the vasopressin analogs on the release of .beta.-endorphin [60617-12-1]-like or ACTH [9002-60-2]-like immunoreactivity was examined The replacement of the proline residue in position 7 by sarcosine or N-methylalanine did not change the maximum effect reached, but increased the EC50 values 20- or 5-fold, resp., when compared with arginine vasopressin [113-79-1]. This decrease in .beta.-endorphin-releasing activity was no longer observed after addnl. removal of the .alpha.-amino group of cysteine in position 1. Since these substitutions are known to reduce vasopressor activity drastically, these data suggest that the .beta.-endorphin-releasing activity of vasopressin can be dissociated from its V1 receptor activity. Vasopressin analogs substituted in position 7 and with deaminopenicillamine or .beta.-mercapto-.beta.,.beta.-cyclopentamethylenepropionic acid in position 1 were found to be weak antagonists of the .beta.-endorphin-releasing activity of vasopressin. Since these analogs are potent antagonists at the V1 receptor, these data suggest that the deaminopenicillamine and, more so, the .beta.-mercapto-.beta.,.beta.-cyclopentamethylenepropionic acid residues in position 1 of vasopressin are strong binding elements at the V1 vasopressin receptor but weak binding elements at the adenohypophyseal vasopressin receptor. A pos. correlation was found between the EC50 values or inhibition consts. of the analogs for their effect on .beta.-endorphin release on the one hand and their potency to displace [3H]arginine vasopressin binding to anterior pituitary membranes on the other hand. Therefore, these data support and extend previous suggestions that the structural requirements of the adenohypophyseal vasopressin receptor differ from those of the V1 vasopressin receptor. In this sense, the adenohypophyseal vasopressin receptor may represent a novel type of vasopressin receptor.
ST vasopressin receptor pituitary anterior lobe; endorphin pituitary vasopressin analog; ACTH pituitary vasopressin analog
IT Pituitary gland, anterior lobe
(ACTH and .beta.-endorphin release by, vasopressin analog effect on, receptors in relation to)
IT Receptors
RL: BIOL (Biological study)
(for vasopressin, of pituitary anterior lobe)
IT Molecular structure-biological activity relationship
(receptor-binding, of vasopressin analogs)
IT Molecular structure-biological activity relationship
(.beta.-endorphin-releasing, of vasopressin analogs)
IT 113-79-1, Arginine vasopressin 11000-17-2D, analogs 84558-77-0, 7-Sarcosine,8-argininevasopressin 84558-78-1, 1-(.beta.-Mercaptopropionic acid),7-sarcosine,8-argininevasopressin **84558-81-6**, 7-N-Methylalanine,8-argininevasopressin **84558-82-7**, 1-.beta.-Mercaptopropionic acid, 7-N-methylalanine,8-argininevasopressin 88463-38-1, 1-Deaminopenicillamine,7-sarcosine,8-argininevasopressin 88463-39-2, 1-.beta.-Mercapto-.beta.,.beta.-cyclopentamethylenepropionic acid,7-sarcosine,8-argininevasopressin **88463-40-5**, 1-Deaminopenicillamine,7-N-methylalanine,8-argininevasopressin **88463-41-6**, 1-.beta.-Mercapto-.beta.,.beta.-cyclopentamethylenepropionic acid, 7-N-methylalanine,8-argininevasopressin
RL: BIOL (Biological study)
(ACTH and .beta.-endorphin release by pituitary anterior lobe response

to, vasopressin receptors in relation to)

IT 11000-17-2
RL: BIOL (Biological study)
(receptors for, of pituitary anterior lobe)

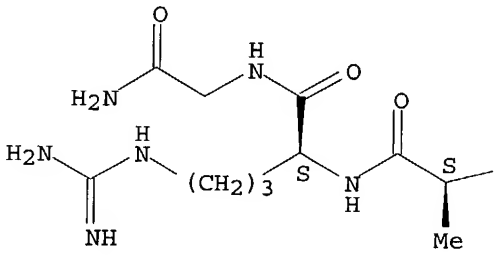
IT 9002-60-2, Adrenocorticotropin, biological studies 60617-12-1
RL: BIOL (Biological study)
(release of, from pituitary anterior lobe, vasopressin analog effect on, structure in relation to)

IT **84558-81-6**, 7-N-Methylalanine,8-argininevasopressin
84558-82-7, 1-.beta.-Mercaptopropionic acid, 7-N-methylalanine,8-argininevasopressin **88463-40-5**, 1-Deaminopenicillamine,7-N-methylalanine,8-argininevasopressin **88463-41-6**, 1-.beta.-Mercapto-.beta.,.beta.-cyclopentamethylenepropionic acid, 7-N-methylalanine,8-argininevasopressin
RL: BIOL (Biological study)
(ACTH and .beta.-endorphin release by pituitary anterior lobe response to, vasopressin receptors in relation to)

RN 84558-81-6 HCAPLUS
CN Vasopressin, 7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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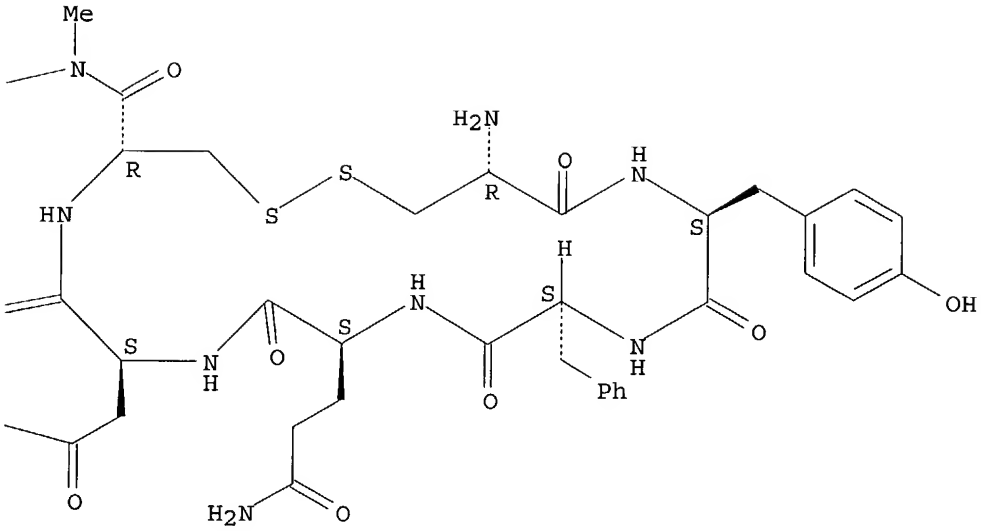
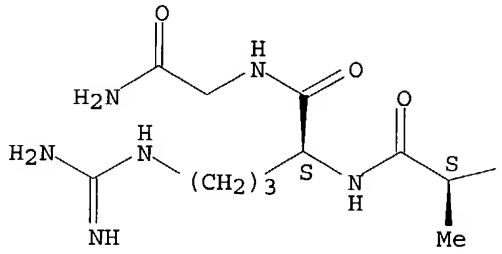


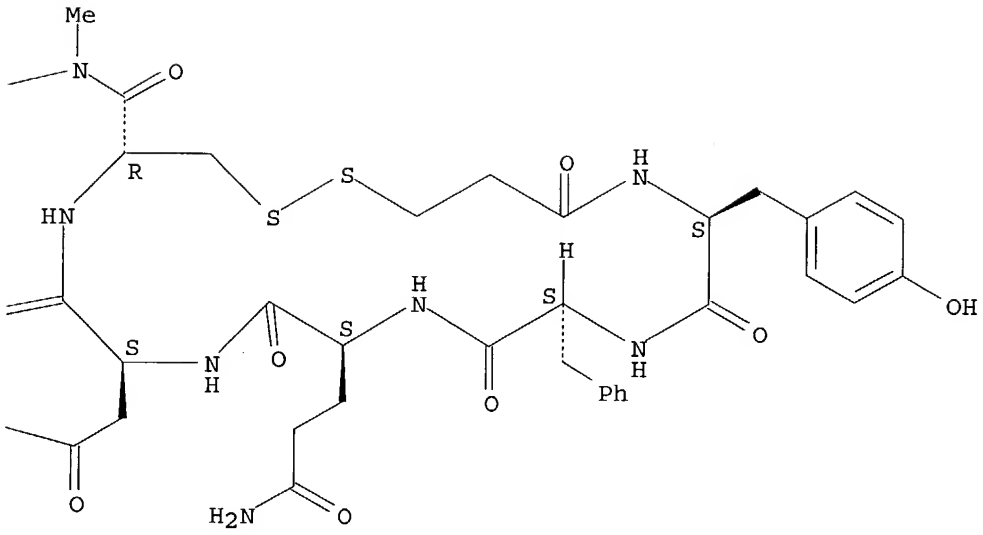
RN 84558-82-7 HCAPLUS
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



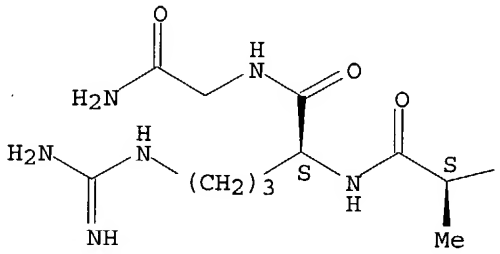
PAGE 1-B



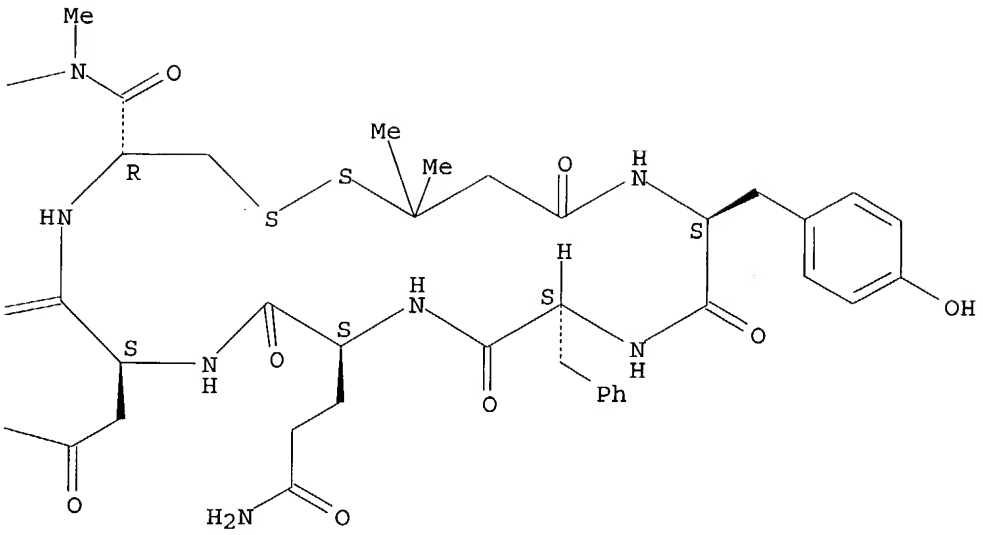
RN 88463-40-5 HCAPLUS
CN Vasopressin, 1-(3-mercapto-3-methylbutanoic acid)-7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



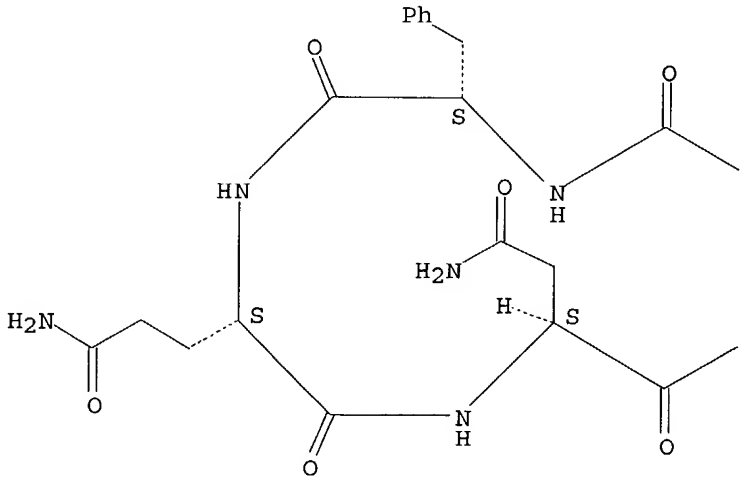
PAGE 1-B



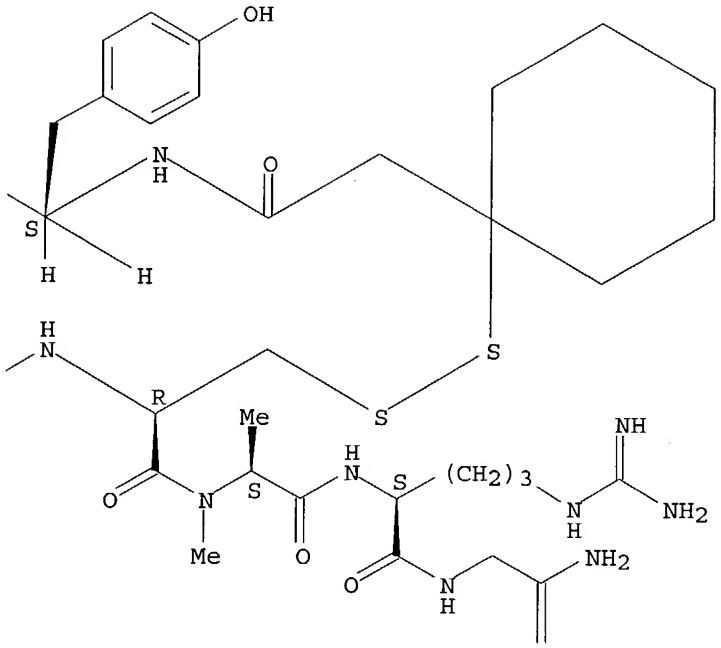
RN 88463-41-6 HCAPLUS
CN Glycinamide, N-[(1-mercaptocyclohexyl)acetyl]-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

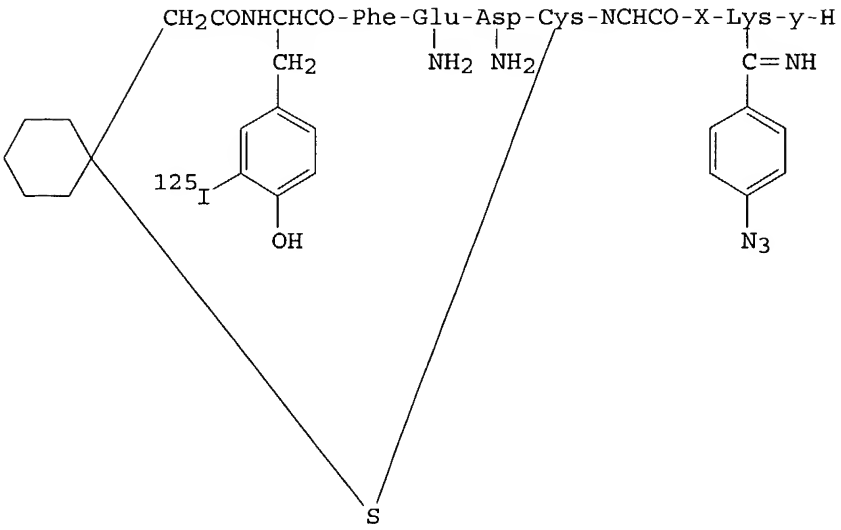


PAGE 1-B



PAGE 2-B

L68 ANSWER 21 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:13062 HCAPLUS
DN 106:13062
ED Entered STN: 24 Jan 1987
TI Iodinated photoreactive vasopressin antagonists. Labelling of hepatic vasopressin receptor subunits
AU Fahrenholz, Falk; Kojro, Elzbieta; Mueller, Michael; Boer, Rainer; Loehr, Reinhold; Grzonka, Zbigniew
CS Max-Planck-Inst. Biophys., Frankfurt, D-6000/70, Fed. Rep. Ger.
SO European Journal of Biochemistry (1986), 161(2), 321-8
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 9
GI



I, y=Gly-NH

II, x=Arg

AB To identify and characterize V1 vasopressin receptors, photoreactive antagonists of the glycogenolytic and vasoconstrictor activity of vasopressin were synthesized. The following analogs with L-3-mercapto-3,3-cyclopentamethylenepropionic acid (Mca) and N-methylalanine (MeAla) in position 1 and 7 of vasopressin (VP) were effective V1 antagonists: [Mca1, D-Tyr2, MeAla7, Lys8]VP (I) [105027-85-8], [Mca1, MeAla7, Arg8, Lys9]VP (II) [105027-86-9] and [Mca1, MeAla7, Arg8, D-Lys9]VP (III) [105181-52-0]. Introduction of the photoreactive 4-azidophenylamidino group into the side chain of lysine in I, II, and III increased to potency (for I a 10-fold increase in the antiglycogenolytic effect and a 5-fold increase in the antivasopressor effect) and binding affinity for the rat hepatic V1 receptor. Monoiodination at tyrosine with 125I resulted in photoreactive antagonists IV [105027-84-7] and V [105047-55-0] which had high specific radioactivity, and roughly the same binding affinity as vasopressin for the rat hepatic V1 receptor (dissociation constant = 0.9-1.8 nM). In photoaffinity labeling expts. with purified rat liver membranes, containing 2-3 pmol V1 receptor/mg protein, the analogs labeled specifically 2 proteins with the relative mol. masses (Mr) of 30,000 and 38,000. Thus, both vasopressin agonists and antagonists can apparently interact with the same 2 subunits of the heterodimeric hepatic V1 receptor. Furthermore, the radioiodinated photoreactive V1 antagonists should be helpful to identify V1 receptor proteins in membranes of other cell types.

ST photoaffinity label vasopressin receptor; radioiodinated photoreactive vasopressin antagonist; structure vasopressin antagonist receptor; liver vasopressin receptor subunit labeling

IT Receptors
RL: BIOL (Biological study)
(for vasopressin, V1, photoaffinity labeling of, of liver, iodinated photoreactive ligands for)

IT Liver, composition
(vasopressin V1 receptors of, photoaffinity labeling of, iodinated photoreactive vasopressin antagonists for)

IT Kidney, metabolism

(vasopressin analogs binding by vasopressin V2 receptors of, characterization of)

IT Molecular structure-biological activity relationship
(antidiuretic, of vasopressin antagonists)

IT Molecular structure-biological activity relationship
(glycogen metabolism-inhibiting, of vasopressin antagonists)

IT Molecular structure-biological activity relationship
(vasodilating, of vasopressin antagonists)

IT 88463-39-2 **88463-41-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antiglycogenolytic activity of, structure in relation to)

IT 11000-17-2DP, iodinated photoreactive analogs
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and V1 receptor affinity of)

IT 105027-87-0P 105047-56-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and iodination and vasopressin receptor affinity of)

IT 105027-84-7P 105027-88-1P 105027-89-2P 105027-90-5P 105047-55-0P
105047-57-2P 105047-58-3P 105181-53-1P 105223-59-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and vasopressin receptor affinity of)

IT 105027-85-8P 105027-86-9P 105181-52-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 62409-36-3, Methyl-4-azidobenzoimidate hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with vasopressin analog)

IT 53053-08-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with vasopressin analogs)

IT 113-79-1, Arginine vasopressin
RL: PROC (Process)
(receptor binding of, in kidney and liver, structure in relation to)

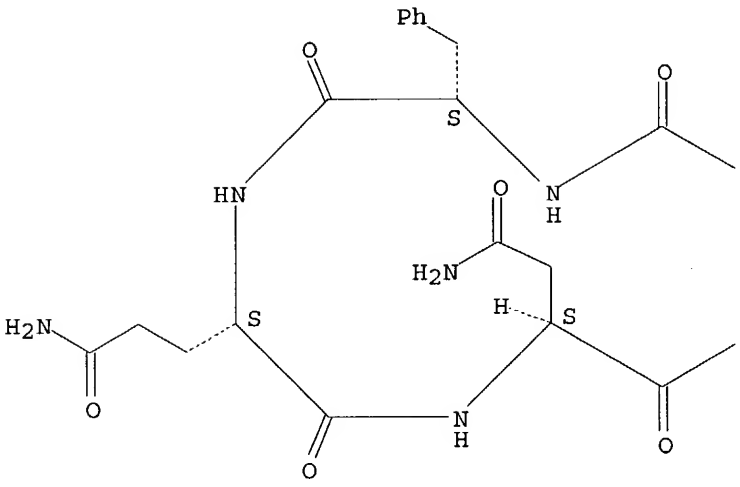
IT **88463-41-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antiglycogenolytic activity of, structure in relation to)

RN 88463-41-6 HCAPLUS

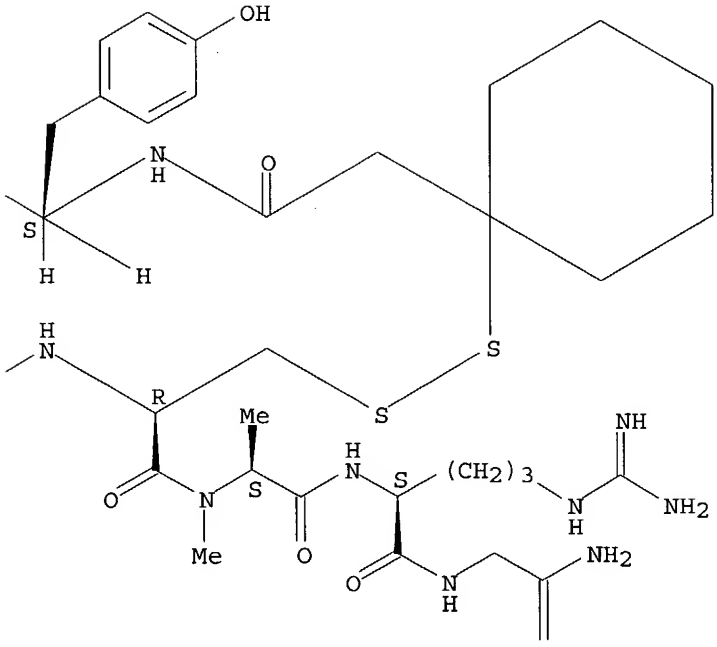
CN Glycinamide, N-[(1-mercaptocyclohexyl)acetyl]-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



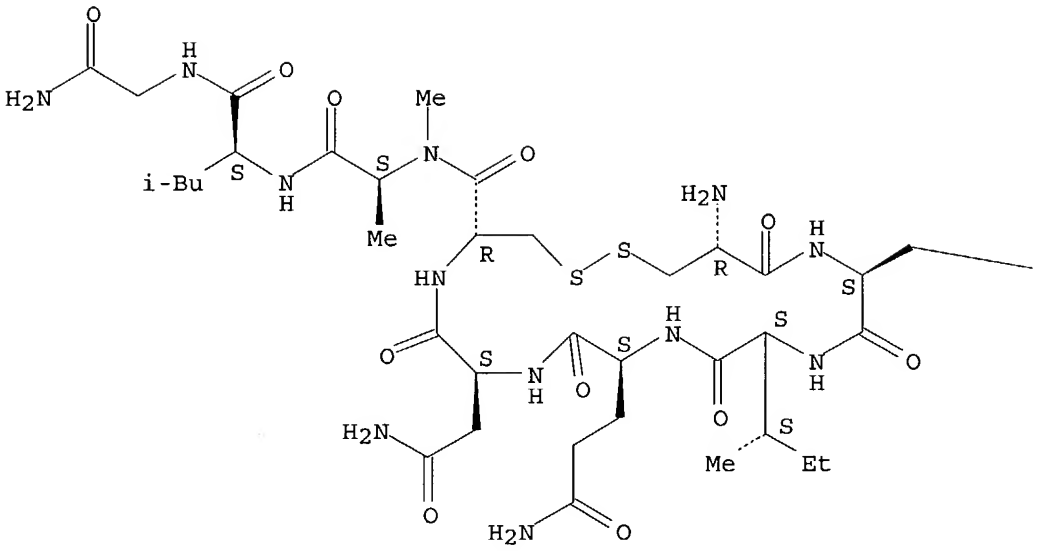
PAGE 2-B

Searched by Noble Jarrell

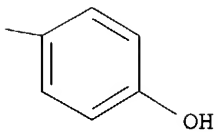
L68 ANSWER 22 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1986:619172 HCAPLUS
DN 105:219172
ED Entered STN: 26 Dec 1986
TI Binding studies with rat myometrial and mammary gland membranes on effects of manganese on relative affinities of receptors for oxytocin analogs
AU Soloff, Melvyn S.; Grzonka, Zbigniew
CS Dep. Biochem., Med. Coll. Ohio, Toledo, OH, 43699, USA
SO Endocrinology (1986), 119(4), 1564-9
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
AB The effects of Mn2+ on the ability of 7-glycine oxytocin derivs. to inhibit the binding of 3H-labeled oxytocin [50-56-6] to receptor sites on rat uterine myometrial and mammary gland plasma membranes were measured. A generally good correlation was found between the ability of the analogs to inhibit [3H]OT binding to both receptor systems and their biol. potencies. An increase in Mn2+ concentration from 1 to 10 mM enhanced the affinity of uterine membranes for the analogs, in inverse proportion to their potencies. This selective enhancement occurred regardless of the structural modification of the peptide. Evidently, the metal ion effect occurs at the receptor level and is not a property of the peptide per se. In contrast to the uterus, the affinities of mammary gland receptors for 2 low potency analogs were unaffected by increased Mn2+ concns. Apparently, Mn2+ allows the conformation of the myometrial receptor to adapt to less well-fitting ligands. Although the metal ion effects on mammary gland receptors are more difficult to interpret, it is clear that uterine and mammary gland receptors are different with respect to the mechanisms of interaction with peptides.
ST oxytocin analog binding mammary uterus manganese
IT Mammary gland
(oxytocin analogs binding by, manganese effect on)
IT Cell membrane
Receptors
RL: BIOL (Biological study)
(oxytocin analogs binding by, of mammary gland and uterus, manganese effect on)
IT Uterus, metabolism
(myometrium, oxytocin analogs binding by, manganese effect on)
IT 7439-96-5, biological studies
RL: BIOL (Biological study)
(oxytocin analogs binding by mammary gland and uterus in response to)
IT 50-56-6D, analogs 19748-53-9 77225-24-2 84558-69-0
84558-73-6 84558-74-7 86969-94-0 **86969-96-2**
RL: BIOL (Biological study)
(receptor binding of, in mammary gland and uterus myometrium, manganese effect on)
IT 50-56-6, biological studies
RL: BIOL (Biological study)
(receptors for, of mammary gland and uterus myometrium, manganese effect on)
IT **84558-73-6 84558-74-7 86969-96-2**
RL: BIOL (Biological study)
(receptor binding of, in mammary gland and uterus myometrium, manganese effect on)
RN 84558-73-6 HCAPLUS
CN Oxytocin, 7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



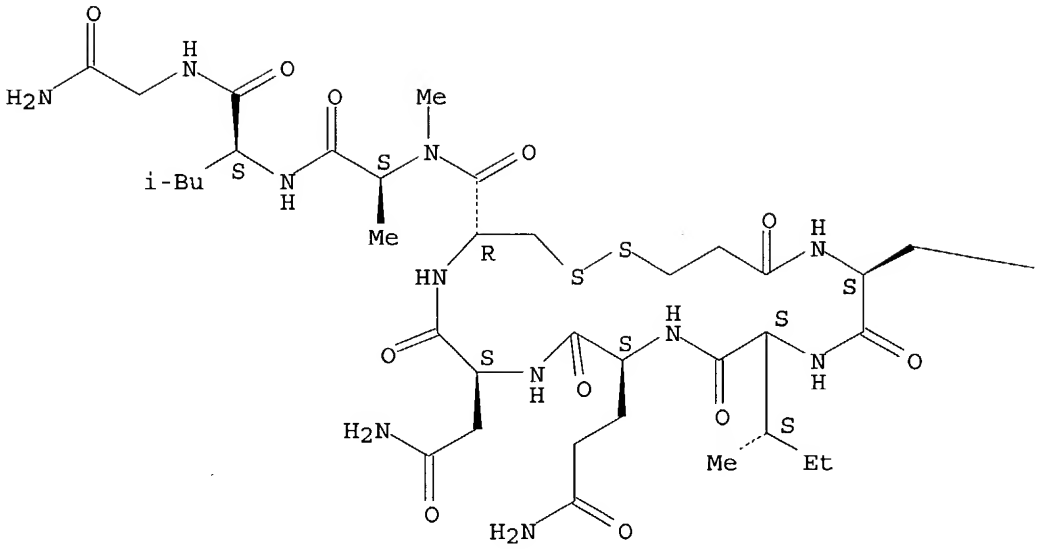
PAGE 1-B



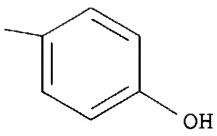
RN 84558-74-7 HCAPLUS
CN Oxytocin, 1-(3-mercaptopropanoic acid)-7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



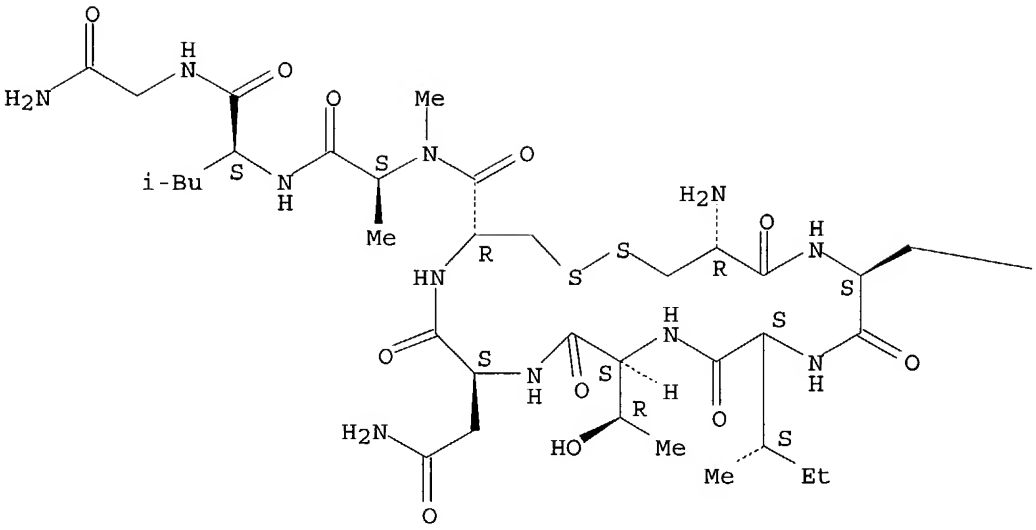
PAGE 1-B



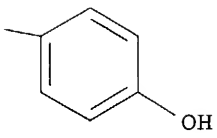
RN 86969-96-2 HCAPLUS
CN Oxytocin, 4-L-threonine-7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

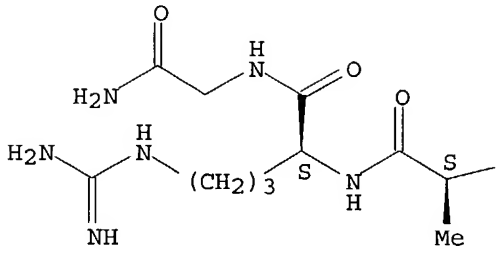


L68 ANSWER 23 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1986:69148 HCAPLUS
DN 104:69148
ED Entered STN: 08 Mar 1986
TI Arginine-vasopressin analogs with high antidiuretic/vasopressor selectivity. Synthesis, biological activity and receptor binding affinity of arginine-vasopressin analogs with substitutions in positions 1, 2, 4, 7, and 8
AU Grzonka, Zbigniew; Kasprzykowski, Franciszek; Kojro, Elzbieta; Darlak, Krzysztof; Melin, Per; Fahrenholz, Falk; Crause, Peter; Boer, Rainer
CS Inst. Chem., Univ. Gdansk, Gdansk, 80-952, Pol.
SO Journal of Medicinal Chemistry (1986), 29(1), 96-9
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)

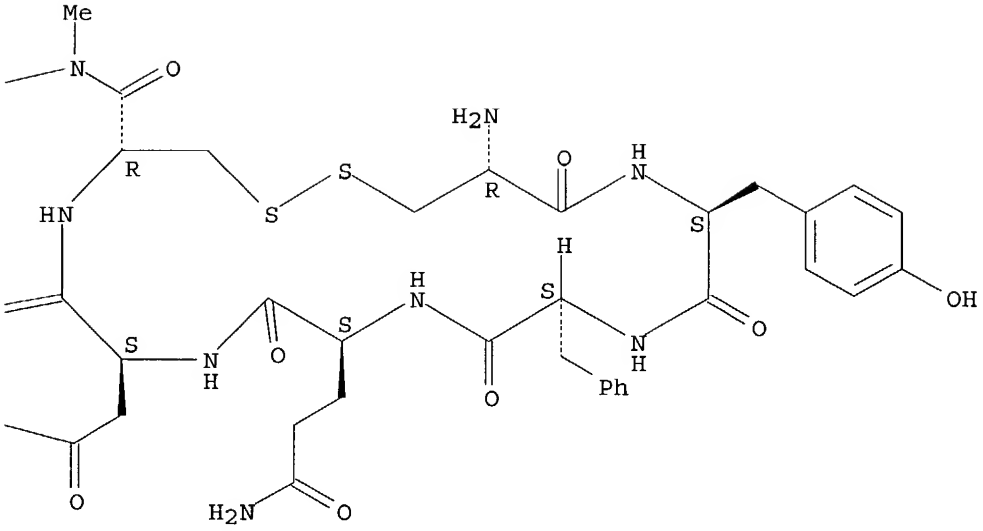
Section cross-reference(s): 2
OS CASREACT 104:69148
AB In a search for more selective agonists of arginine-vasopressin (AVP), 10 analogs of [Sar7]- and [MeAla7]AVP with addnl. substitutions in positions 1 (.beta.-mercaptopropionic acid), 2 (phenylalanine), 4 (valine), or 8 (D-arginine) were prepared and tested for antidiuretic and vasopressor activities. All analogs are characterized by a relatively high antidiuretic activity and by a sharp decrease in pressor activity. Their antidiuretic/vasopressor selectivities were generally 2-3 orders higher than that of the parent hormone. The additivity of the effects of changes in positions 1, 2, 4, and 8 combined with the sarcosine or N-methylalanine substitutions in position 7 on the biol. activity is observed Binding affinities of AVP analogs to plasma membranes from bovine kidney inner medulla and from rat liver containing specific vasopressin receptors were also determined Generally, these analogs retained high binding affinities to renal vasopressin receptors, and they are characterized by a large decrease in binding affinities to hepatic vasopressin receptors, which share characteristics with vasopressor receptors.
ST arginine vasopressin analog prepn antidiuretic vasopressor
IT Merrifield synthesis
(of arginine-vasopressin analogs)
IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(vasopressin-related, preparation and antidiuretic-vasopressor and receptor binding activities of)
IT Molecular structure-biological activity relationship
(antidiuretic, of arginine-vasopressin analogs)
IT **84558-81-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(antidiuretic-vasopressin activity of)
IT 42417-62-9
RL: PROC (Process)
(binding of, to bovine kidney membrane)
IT 113-79-1DP, analogs 97868-94-5P 97868-95-6P 97868-96-7P
97884-18-9P 97906-81-5P 97906-82-6P 97906-83-7P 97906-84-8P
98525-39-4P 98525-40-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antidiuretic-vasopressor and receptor binding activities of)
IT 98509-76-3P 98509-77-4P 98509-78-5P 98525-41-8P 98525-42-9P
98539-79-8P 98575-33-8P 98575-34-9P 98575-35-0P 98632-66-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection-oxidative cyclization of)
IT 4530-20-5D, resin-bound
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase peptide synthesis with)
IT **84558-81-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(antidiuretic-vasopressin activity of)
RN 84558-81-6 HCAPLUS
CN Vasopressin, 7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L68 ANSWER 24 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1985:406703 HCAPLUS
DN 103:6703
ED Entered STN: 12 Jul 1985
TI Conformational preferences and binding to neurophysins of oxytocin analogs with sarcosine or N-methylalanine in position 7
AU Grzonka, Zbigniew; Mishra, P. K.; Bothner-By, A. A.
CS Inst. Chem., Univ. Gdansk, Gdansk, Pol.

Searched by Noble Jarrell

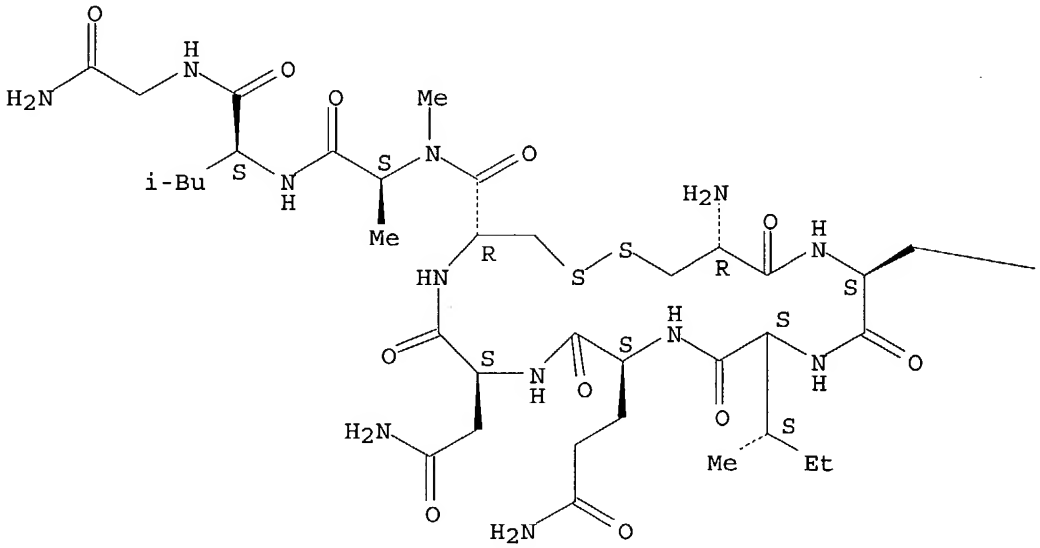
SO International Journal of Peptide & Protein Research (1985), 25(4), 375-81
CODEN: IJPPC3; ISSN: 0367-8377
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 22

AB The 600 MHz proton NMR spectra of (sarcosyl7)-oxytocin (I) and (N-methylalanyl7)-oxytocin (II) in 2H2O solution have been recorded and completely assigned. In each case the spectrum indicates the presence of two slowly interconverting conformers, which are the cis-trans isomers about the peptide bond between residues 6 and 7. The trans isomer is energetically favored in both cases. When neurophysin is added to a solution of I or II at pH 3.0, the proportion of minor conformer remains constant, indicating that the cis and trans conformers are equally tightly bound to the protein.

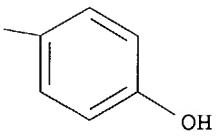
ST oxytocin analog conformation binding neurophysin; sarcosine oxytocin conformation binding neurophysin; methylalanine oxytocin conformation binding neurophysin
IT Neurophysins
RL: PROC (Process)
(binding of, with sarcosine- and methylalanine-oxytocin analogs)
IT Conformation and Conformers
(of sarcosine- and methylalanine-oxytocin analogs)
IT Molecular structure-property relationship
(NMR, of sarcosine- and methylalanine-oxytocin analogs)
IT 50-56-6D, analogs. 77225-24-2 **84558-73-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(conformation and neurophysin-binding properties of)
IT **84558-73-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(conformation and neurophysin-binding properties of)
RN 84558-73-6 HCAPLUS
CN Oxytocin, 7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L68 ANSWER 25 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1984:417564 HCAPLUS
DN 101:17564
ED Entered STN: 21 Jul 1984
TI Interactions of vasopressin agonists and antagonists with membrane receptors
AU Fahrenholz, Falk; Boer, Rainer; Crause, Peter; Fritzsch, Gunter; Grzonka, Zbigniew
CS Max-Planck-Inst. Biophys., Frankfurt/Main, D-6000/70, Fed. Rep. Ger.
SO European Journal of Pharmacology (1984), 100(1), 47-58
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
AB Plasma membranes containing 1 class of noncooperative binding sites for 3H-labeled [8-arginine]vasopressin [113-79-1] were isolated from bovine kidney inner medulla and from rat liver. By using a weighted, nonlinear least squares fit to logistic curves, the binding parameters of 8 vasopressin agonists and antagonists were determined in competition expts. Vasopressin analogs with sarcosine or N-methyl-L-alanine in position 7 instead of proline showed a high ratio of antidiuretic to vasopressor activity. These analogs retained a high-binding affinity to the renal vasopressin receptor with apparent dissociation consts. KD in the order proline < sarcosine < methylalanine. In contrast, the affinity to the hepatic vasopressin receptor, which shares characteristics with vasopressor receptors, was drastically reduced with KD values being in the order proline .mchlt. N-methylalanine < sarcosine. By combining the substitutions at position 7 with substitutions of cysteine in position 1 by either deaminopenicillamine or .beta.-mercapto-.beta.,.beta.-cyclopentamethylenepropionic acid, inhibitors of the oxytocoic acid and vasopressor responses were obtained. These addnl. substitutions at position 1 led to a drastic decrease in the binding affinity to the vasopressin receptor in bovine kidney. The intrinsic activity of these analogs to stimulate the renal vasopressin-sensitive adenylate cyclase [9012-42-4] was strongly reduced or completely lost. In the rat liver system, however, these vasopressin antagonists showed a remarkably increased affinity to vasopressin receptors as compared to analogs substituted only at position 7. GTP reduced the binding affinity of all analogs to the hepatic receptor. Thus, structural activities which influence both the conformational properties of the vasopressin mol. and

the biol. activities of the hormone have strikingly different effects on the interactions of the resulting analogs with physiol. important receptors in the kidney and the liver. These studies may lead to the development of more specific vasopressin agonists and antagonists.

ST vasopressin receptor structure activity

IT Receptors
RL: BIOL (Biological study)
(vasopressin analog binding by, in kidney and liver, structure in relation to)

IT Kidney, composition
Liver, composition
(vasopressin receptor of membranes of, analog binding by)

IT Cell membrane
(vasopressin receptor of, of kidney and liver)

IT Molecular structure-biological activity relationship
(vasopressin receptor-binding, of vasopressin analogs)

IT 113-79-1
RL: PROC (Process)
(receptor binding of, in kidney and liver, structure in relation to)

IT 84558-77-0 84558-78-1 **84558-81-6 84558-82-7**
88463-38-1 88463-39-2 **88463-40-5 88463-41-6**
RL: PROC (Process)
(vasopressin receptor binding of, in kidney and liver, structure in relation to)

IT 9012-42-4
RL: BIOL (Biological study)
(vasopressin-sensitive, of kidney, vasopressin analogs effect on)

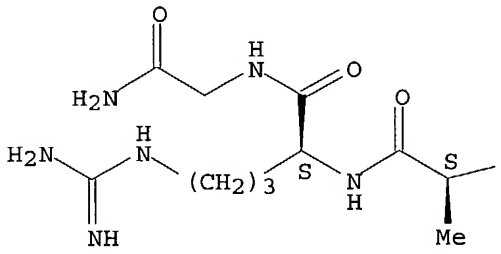
IT **84558-81-6 84558-82-7 88463-40-5 88463-41-6**
RL: PROC (Process)
(vasopressin receptor binding of, in kidney and liver, structure in relation to)

RN 84558-81-6 HCAPLUS

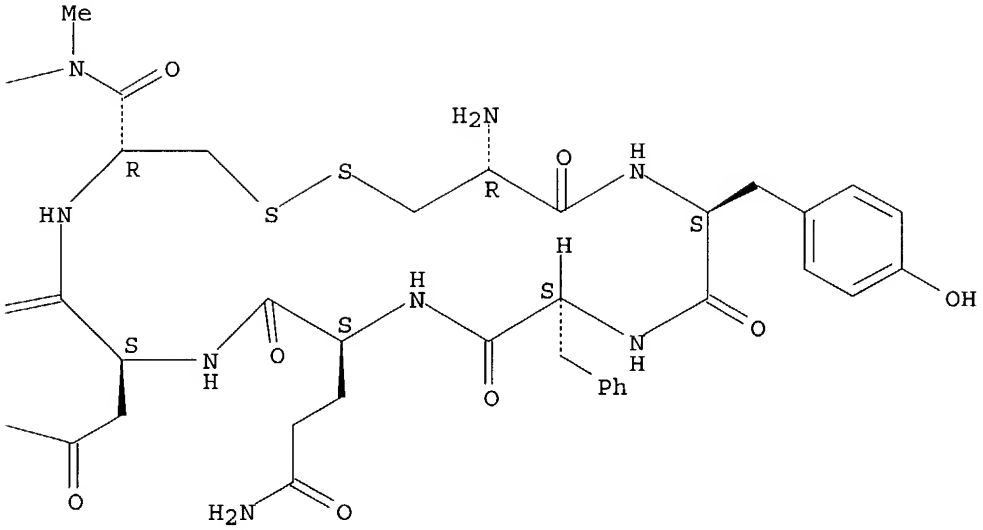
CN Vasopressin, 7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



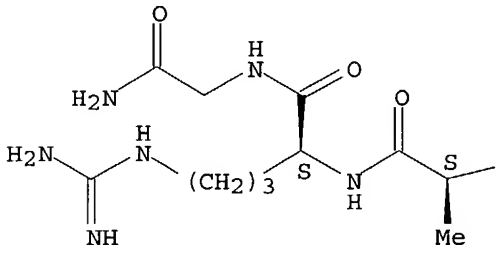
PAGE 1-B



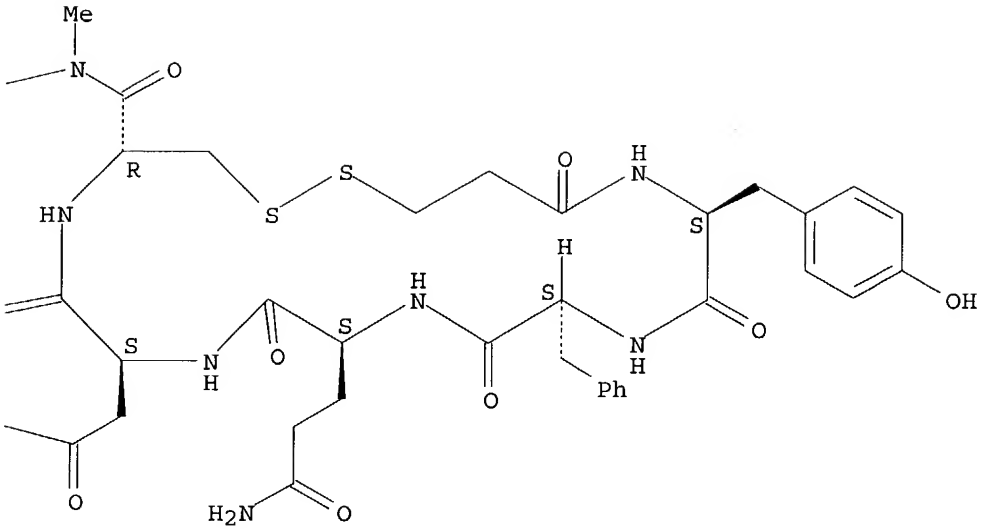
RN 84558-82-7 HCAPLUS
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



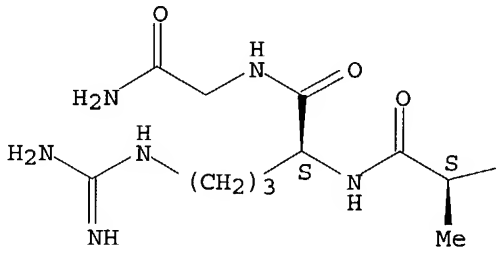
PAGE 1-B

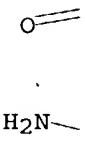


RN 88463-40-5 HCAPLUS
CN Vasopressin, 1-(3-mercapto-3-methylbutanoic acid)-7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

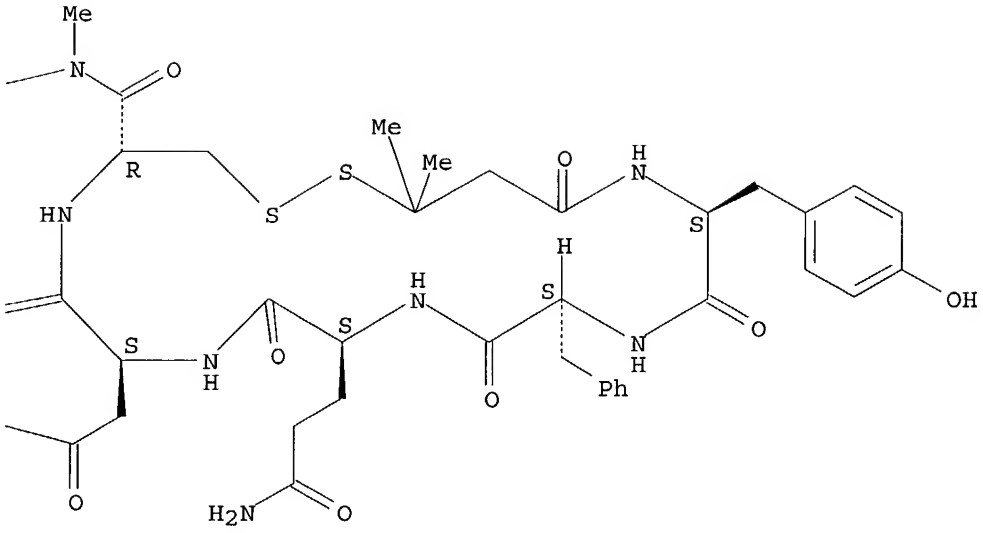
Absolute stereochemistry.

PAGE 1-A





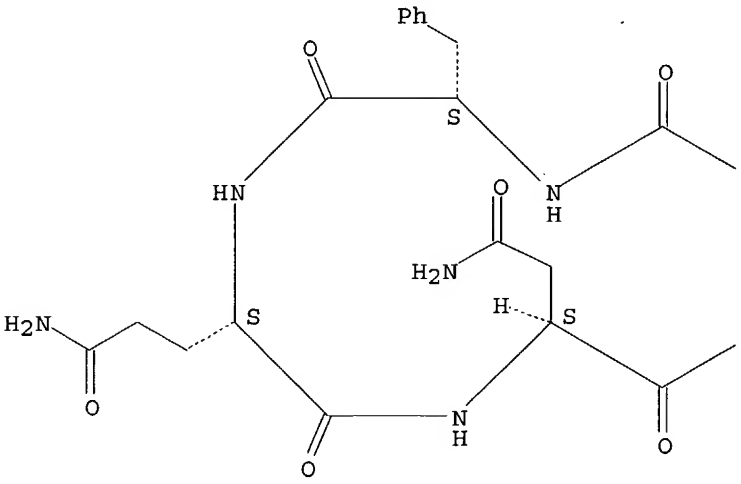
PAGE 1-B



RN 88463-41-6 HCAPLUS
CN Glycinamide, N-[(1-mercaptocyclohexyl)acetyl]-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

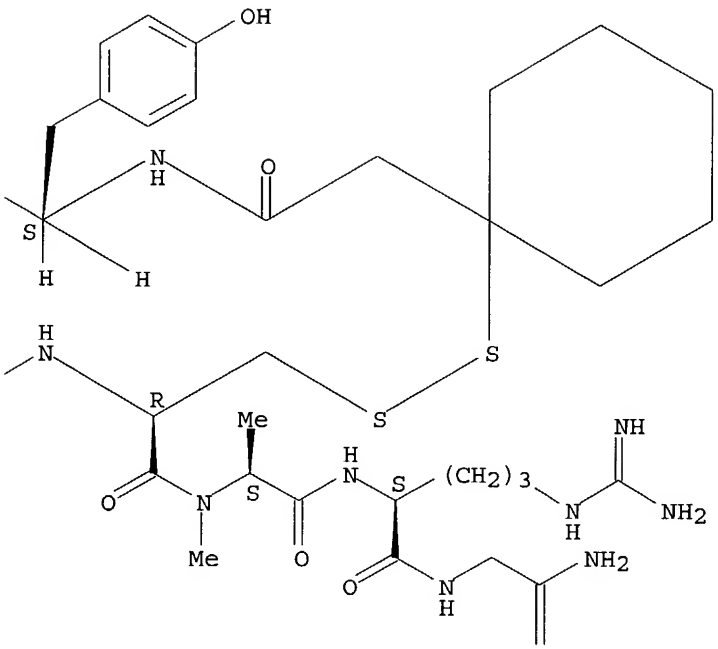
Absolute stereochemistry.

PAGE 1-A



Searched by Noble Jarrell

PAGE 1-B



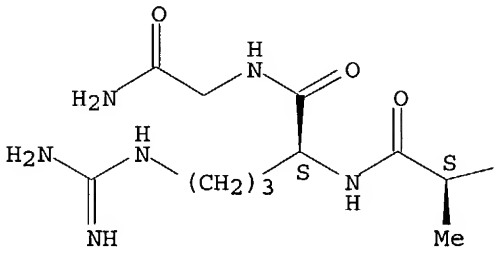
PAGE 2-B

L68 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1984:115143 HCAPLUS
DN 100:115143
ED Entered STN: 12 May 1984
TI Influence of sarcosine or N-methylalanine in position 7 on the antagonistic properties of [1-deaminopenicillamine]- and [1-(.beta.-mercapto-.beta.,.beta.-cyclopentylmethylenepropionic acid)]vasopressin
AU Gazis, Diana; Schwartz, Irving L.; Lammek, B.; Grzonka, Zbigniew
CS Cent. Polypept. Membr. Res., Mount Sinai Sch. Med., New York, NY, USA
SO International Journal of Peptide & Protein Research (1984), 23(1), 78-83
CODEN: IJPPC3; ISSN: 0367-8377
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 34
AB Substituting sarcosine or N-methylalanine for proline in the inhibitory vasopressin analogs of [1-deaminopenicillamine]arginine-vasopressin (dPAVP) and [1-(.beta.-mercapto-.beta.,.beta.-cyclopentylmethylenepropionic acid]-vasopressin [d(CH2)5AVP] had the following effects: milk ejection and antidiuretic activities were severely depressed, pressor antagonism was maintained but weakened somewhat, and antagonism in the uterus in vitro was maintained, but no consistent pattern was seen.

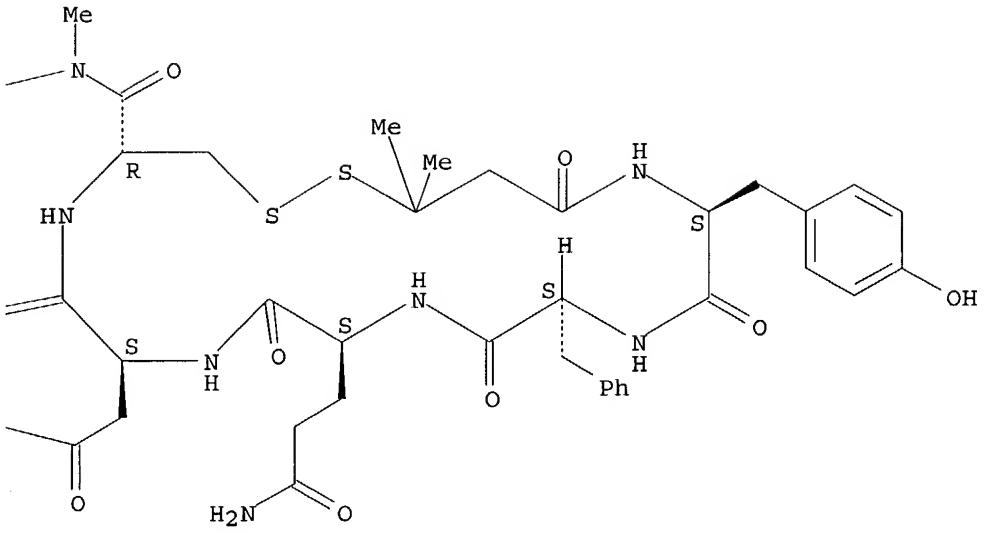
ST vasopressin analog structure activity; peptide prepn
IT Molecular structure-biological activity relationship
(of arginine-vasopressin analogs)
IT 113-79-1D, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(biol. activity of, structure in relation to)
IT 88463-38-1P 88463-39-2P **88463-40-5P 88463-41-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of, structure in relation to)
IT 89273-20-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and deblocking and reoxidn. of)
IT 89273-19-8P 89273-21-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking of)
IT 89273-22-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and reduction and reoxidn. of)
IT **88463-40-5P 88463-41-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of, structure in relation to)
RN 88463-40-5 HCAPLUS
CN Vasopressin, 1-(3-mercapto-3-methylbutanoic acid)-7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



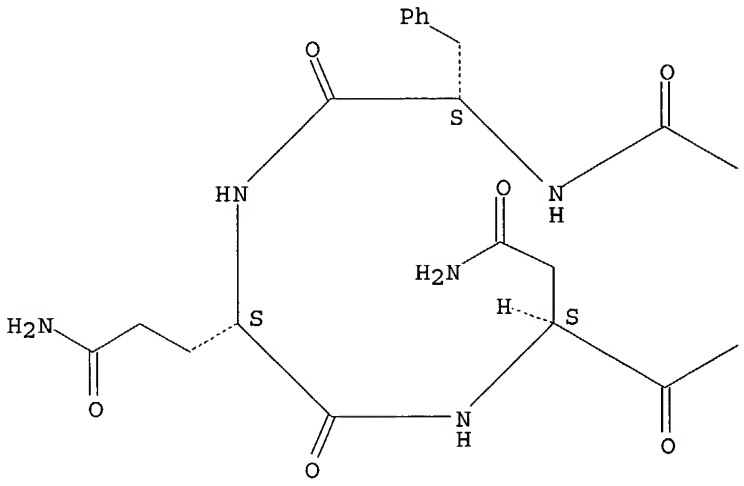
PAGE 1-B



RN 88463-41-6 HCAPLUS
CN Glycinamide, N-[(1-mercaptocyclohexyl)acetyl]-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

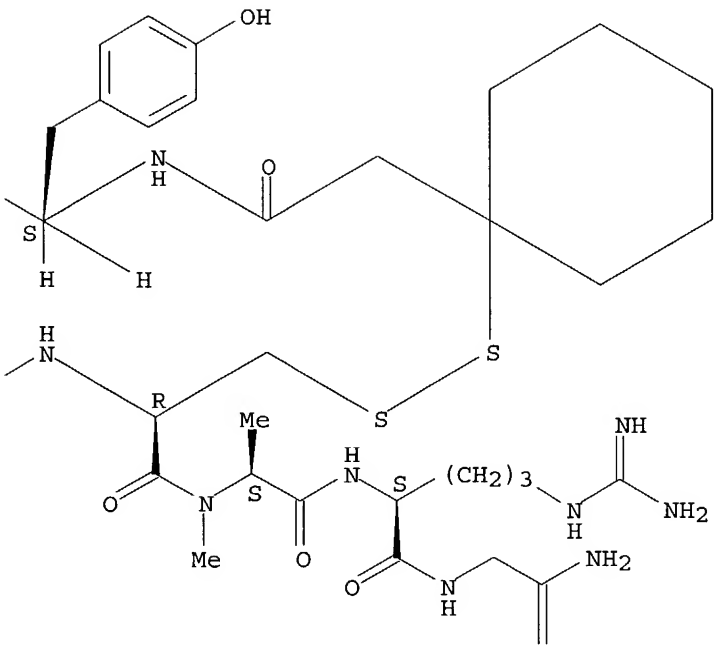
Absolute stereochemistry.

PAGE 1-A



Searched by Noble Jarrell

PAGE 1-B



PAGE 2-B

L68 ANSWER 27 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1984:51985 HCAPLUS
DN 100:51985
ED Entered STN: 12 May 1984
TI Synthesis of new active and highly selective analogs of oxytocin and arginine-vasopressin
AU Grzonka, Zbigniew; Kasprzykowski, Franciszek; Lammek, Bernard; Gazis, Diana; Schwartz, Irving L.
CS Inst. Chem., Univ. Gdansk, Gdansk, 80-952, Pol.
SO Pept., Proc. Eur. Pept. Symp., 17th (1983), Meeting Date 1982, 445-8. Editor(s): Blaha, Karel; Malon, Petr. Publisher: de Gruyter, Berlin, Fed. Rep. Ger.
CODEN: 50GFAA
DT Conference
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
AB The title analogs resulted from replacement of a proline residue at position 7 with either sarcosine or N-methylalanine. Positions 1 and 4 were also substituted. Substitution of sarcosine at position 7 gave analogs with higher oxytocic and milk ejection activities than did substitution of N-methylalanine.
ST oxytocin analog; arginine vasopressin analog; proline analog oxytoxin vasopressin; methylalanine analog oxytocin vasopressin; sarcosine oxytocin

analog prepn oxytocic

IT Molecular structure-biological activity relationship
(oxytocic, of proline and methylalanine analogs)

IT 77225-24-2P 84558-69-0P **84558-73-6P 84558-74-7P**
84558-77-0P 84558-78-1P **84558-81-6P 84558-82-7P**
86969-94-0P **86969-96-2P** 88463-38-1P 88463-39-2P
88463-40-5P 88463-41-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of)

IT 50-56-6DP, analogs 113-79-1P
RL: PREP (Preparation)
(synthesis and biol. activity of)

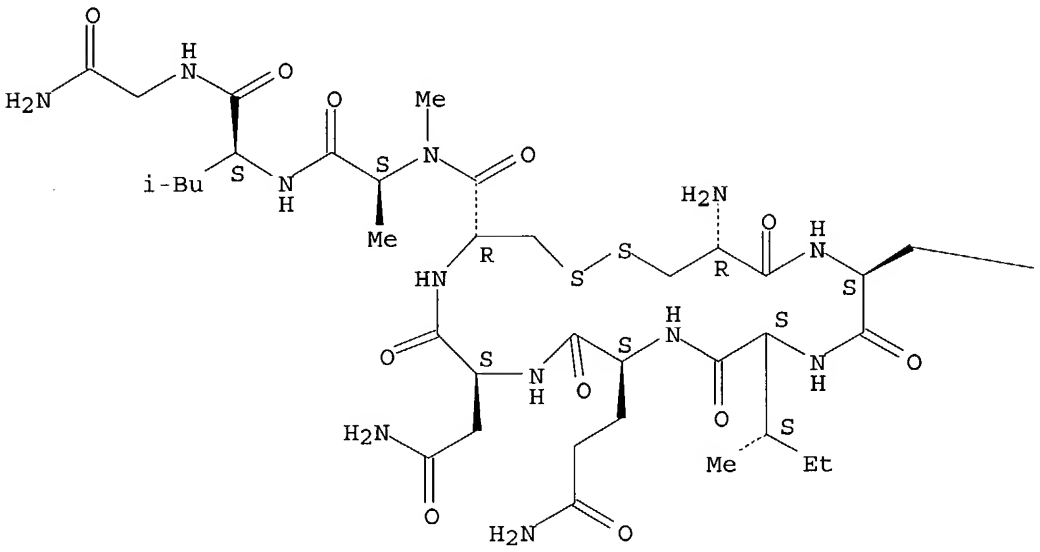
IT **84558-73-6P 84558-74-7P 84558-81-6P**
84558-82-7P 86969-96-2P 88463-40-5P
88463-41-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of)

RN 84558-73-6 HCAPLUS

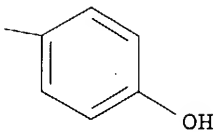
CN Oxytocin, 7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



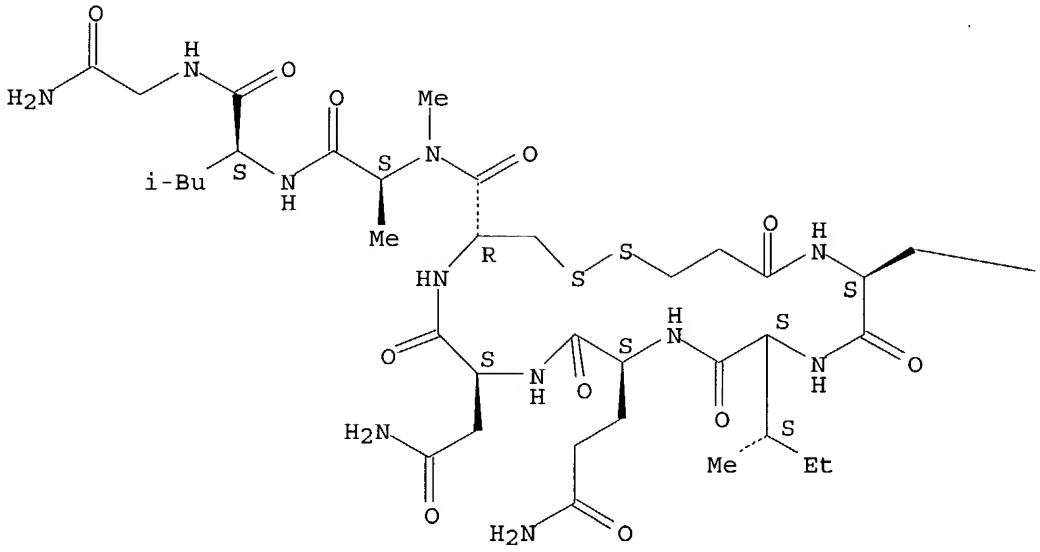
PAGE 1-B



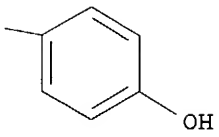
RN 84558-74-7 HCAPLUS
CN Oxytocin, 1-(3-mercaptopropanoic acid)-7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



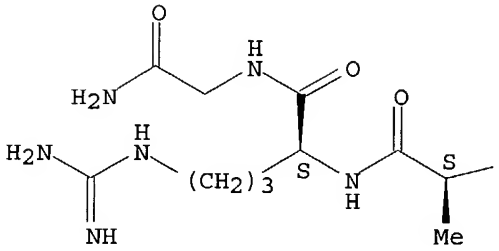
PAGE 1-B



RN 84558-81-6 HCAPLUS
CN Vasopressin, 7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

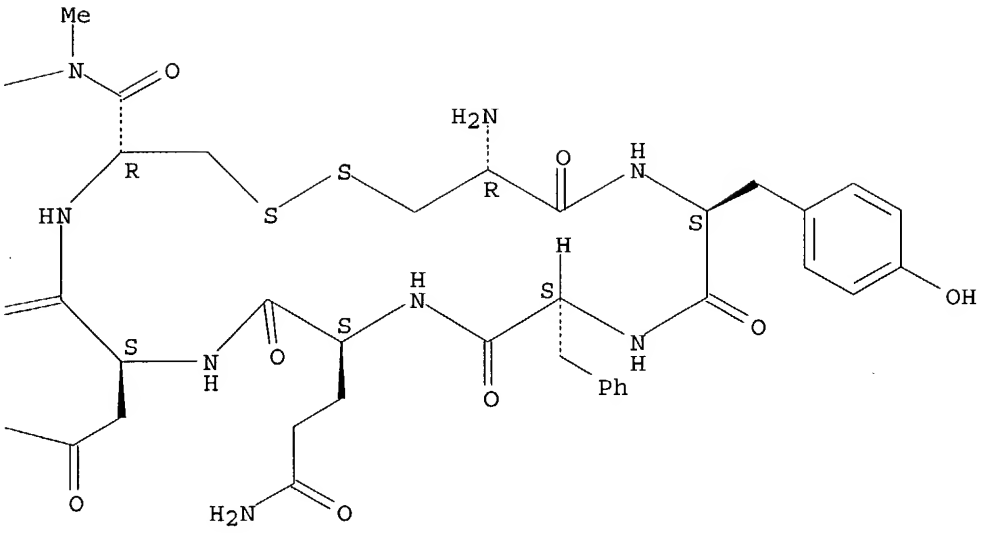
Absolute stereochemistry.

PAGE 1-A



Searched by Noble Jarrell

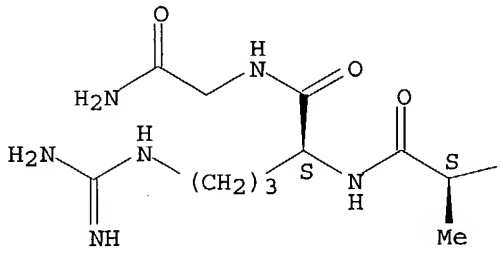
PAGE 1-B



RN 84558-82-7 HCAPLUS
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

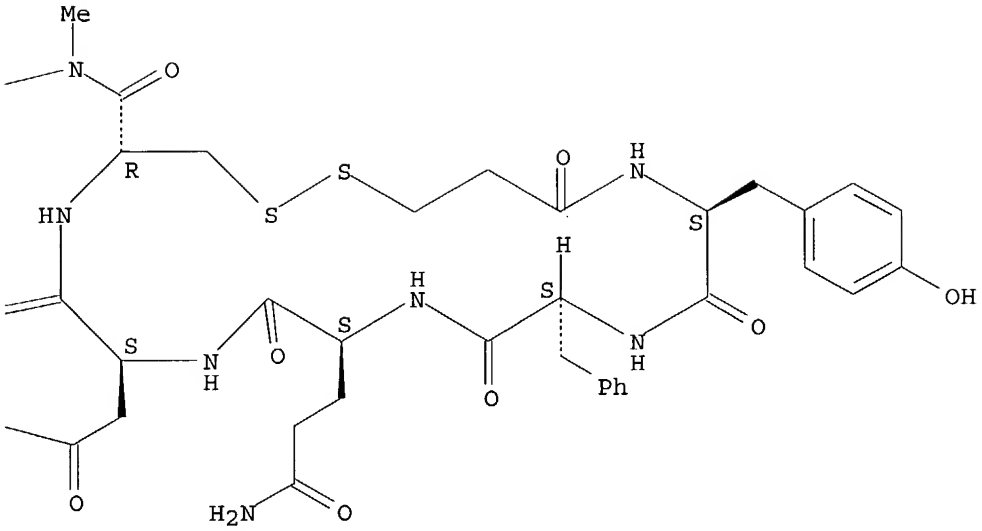
Absolute stereochemistry.

PAGE 1-A



Searched by Noble Jarrell

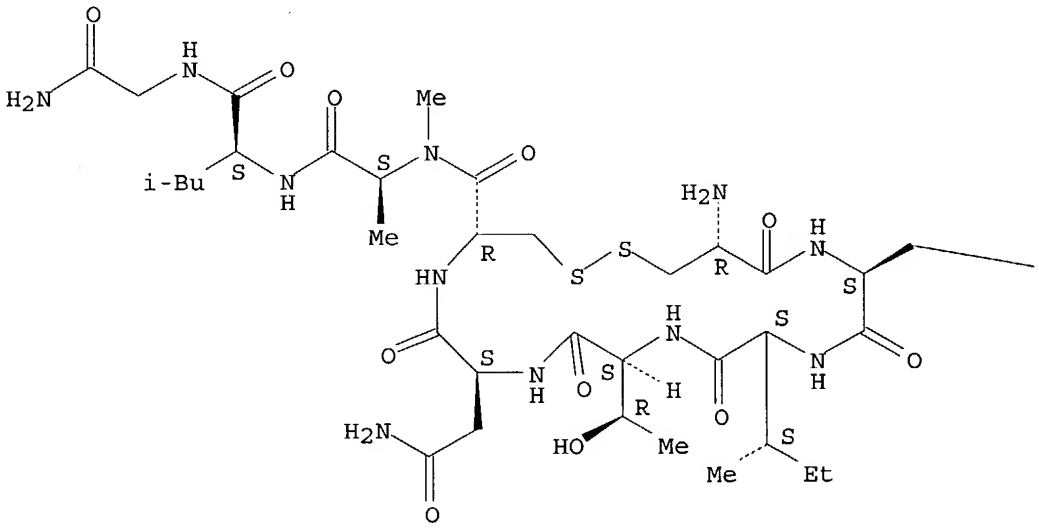
PAGE 1-B



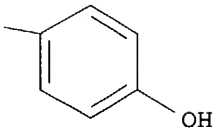
RN 86969-96-2 HCAPLUS
CN Oxytocin, 4-L-threonine-7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



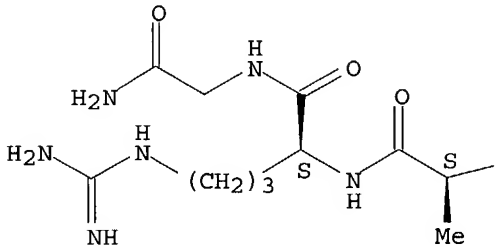
PAGE 1-B



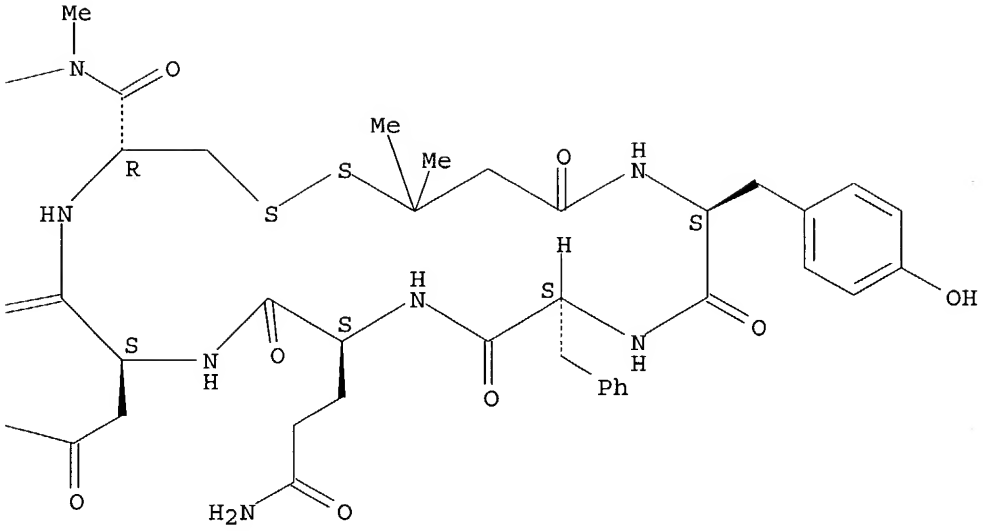
RN 88463-40-5 HCAPLUS
CN Vasopressin, 1-(3-mercapto-3-methylbutanoic acid)-7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



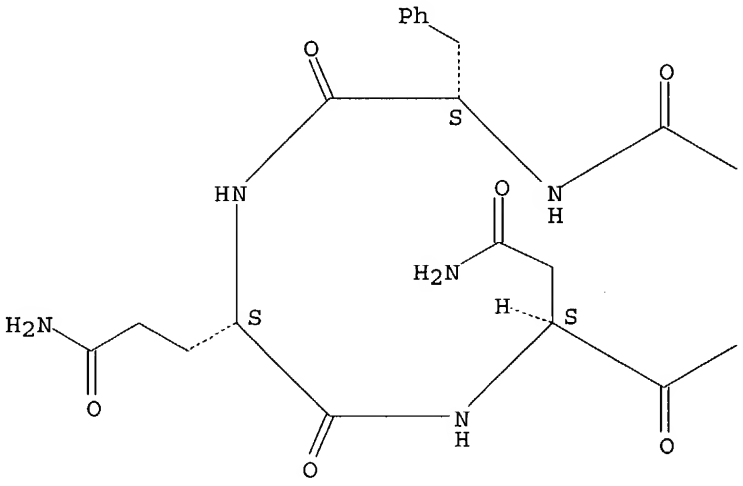
PAGE 1-B



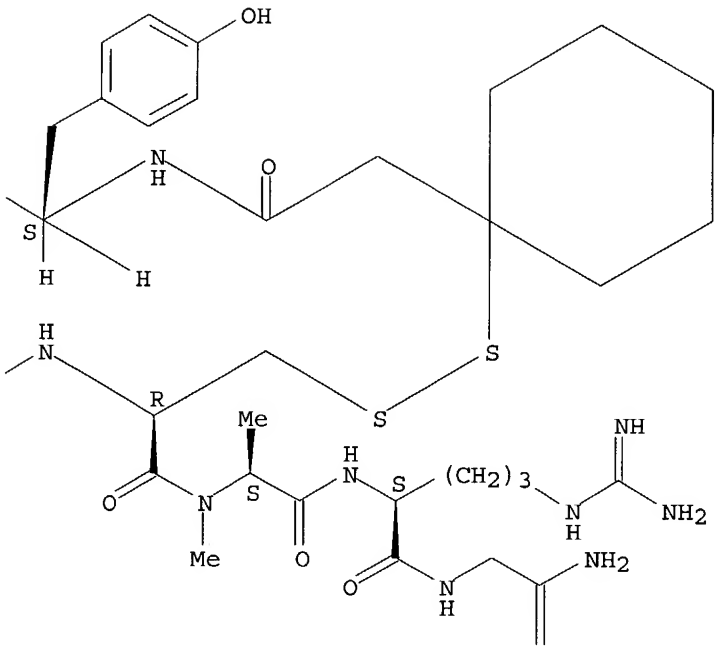
RN 88463-41-6 HCAPLUS
CN Glycinamide, N-[(1-mercaptocyclohexyl)acetyl]-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 2-B

L68 ANSWER 28 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1983:595396 HCAPLUS
DN 99:195396
ED Entered STN: 12 May 1984
TI Synthesis and some pharmacological properties of [4-threonine,7-sarcosine]oxytocin, a peptide with high oxytocic potency, and of [4-threonine,7-N-methylalanine]oxytocin
AU Grzonka, Zbigniew; Lammek, Bernard; Gazis, Diana; Schwartz, Irving L.
CS Inst. Chem., Univ. Gdansk, Gdansk, 80-952, Pol.
SO Journal of Medicinal Chemistry (1983), 26(12), 1786-7
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2
AB Title oxytocin analogs were prepared by the solid phase method and their pharmacol. properties investigated. [Thr4,Sar7]oxytocin exhibits high biol. activity (uterotonic activity of 1174 .+-. 104 and milk ejection activity of 731 .+-. 57 units/mg) and high selectivity for oxytocin-like relative to vasopressin-like activities (antidiuretic activity of 0.037 .+-. 0.012 unig/mg and undetectable pressor activity). [Thr4,MeAla7]oxytocin was characterized by markedly lower biol. activities. The activities were compared to those for oxytocin.
ST oxytocin analog prepn pharmacol; Merrifield synthesis oxytocin analog

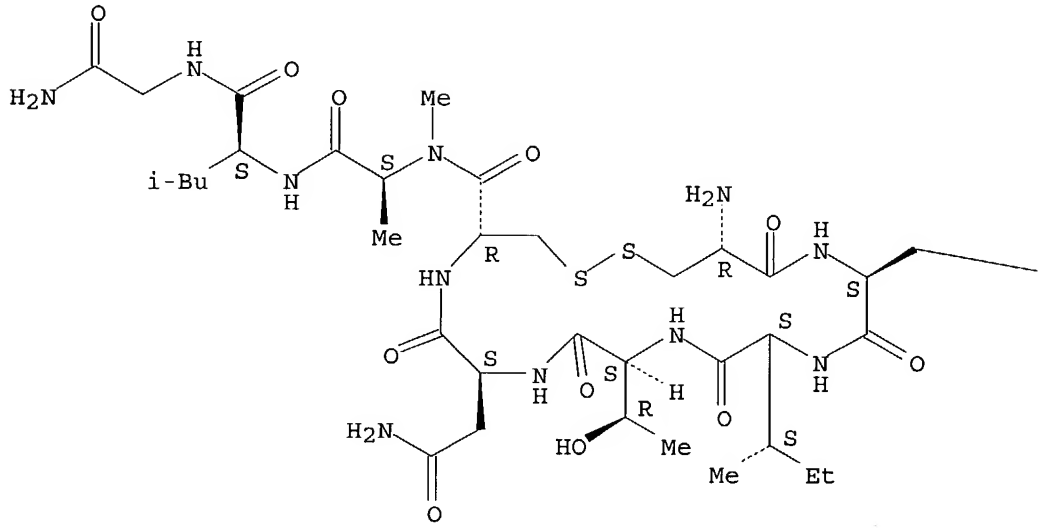
IT Merrifield synthesis
(of oxytoxicn analogs)
IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(oxytocin-related, preparation and biol. activities of)
IT Molecular structure-biological activity relationship
(oxytocic, of oxytocin analogs)
IT 50-56-6DP, analogs 86969-95-1P **86969-97-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activities of)
IT 86969-92-8P 86969-93-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection-oxidative cyclization of)
IT 86969-98-4DP, resin bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and resin cleavage of, by ammonolysis of)
IT 4530-20-5D, resin bound
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase peptide synthesis with)
IT **86969-97-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activities of)
RN 86969-97-3 HCAPLUS
CN Oxytocin, 4-L-threonine-7-(N-methyl-L-alanine)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

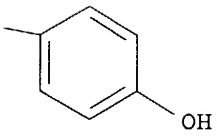
CRN 86969-96-2
CMF C41 H65 N11 O12 S2

Absolute stereochemistry.

PAGE 1-A

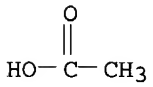


PAGE 1-B



CM 2

CRN 64-19-7
CMF C2 H4 O2



L68 ANSWER 29 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1983:126613 HCAPLUS
DN 98:126613
ED Entered STN: 12 May 1984
TI Synthesis and some pharmacological properties of oxytocin and vasopressin analogs with sarcosine or N-methyl-L-alanine in position 7
AU Grzonka, Zbigniew; Lammek, Bernard; Kasprzykowski, Franciszek; Gazis, Diana; Schwartz, Irving L.
CS Inst. Chem., Univ. Gdansk, Gdansk, 80-952, Pol.
SO Journal of Medicinal Chemistry (1983), 26(4), 555-9
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2
GI For diagram(s), see printed CA Issue.
AB Oxytocin analogs I [R = H2N, H; X = MeGly (Sar), MeAla] and vasopressin analogs II (R1 = H2N, H; X1 = Sar, MeAla) were prepared by the solid-phase method. The final protected peptidyl resins were cleaved by ammonolysis to give the protected peptide amides, which were deblocked by Na/NH3 and then cyclized by oxidation with K3FeCN6 to give the above analogs. I and II exhibited potent antidiuretic or uterotonic activities, these analogs were selective in their action. I with X = Sar had higher oxytocic and milk-ejecting activities than those I with X = MeAla. However, the MeAla7 analogs of II were more potent than the Sar7 analogs with respect to pressor activity.
ST sarcosine oxytocin vasopressin; methylalanine oxytocin vasopressin;

oxytocin sarcosine methylalanine; vasopressin sarcosine methylalanine; antidiuretic sarcosine methylalanine oxytocin; uterotonic sarcosine methylalanine oxytocin; pressor sarcosine methylalanine vasopressin; milk ejecting sarcosine methylalanine oxytocin; structure activity oxytocin vasopressin

IT Uterus
(contraction of, methylalanine- or sarcosine-containing oxytocin and vasopressin analogs as stimulants for)

IT Antidiuretics
(methylalanine- or sarcosine-containing oxytocin and vasopressin analogs)

IT Antihypotensives
(methylalanine- or sarcosine-containing vasopressin analogs)

IT Conformation and Conformers
(of sarcosine or methylalanine containing oxytocin analogs)

IT Lactation
(promotion of, by methylalanine- or sarcosine-containing oxytocin and vasopressin analogs)

IT Molecular structure-biological activity relationship
(antidiuretic, of methylalanine-sarcosine-containing oxytocin and vasopressin analogs)

IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(methylalanine-containing, oxytocin- and vasopressin-related, preparation and biol. activities of)

IT Molecular structure-biological activity relationship
(milk-ejecting, of methylalanine-sarcosine-containing oxytocin and vasopressin analogs)

IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(sarcosine-containing, oxytocin- and vasopressin-related, preparation and biol. activities of)

IT Molecular structure-biological activity relationship
(uterotonic, of methylalanine-sarcosine-containing oxytocin and vasopressin analogs)

IT Molecular structure-biological activity relationship
(vasopressor, of methylalanine- or sarcosine-containing vasopressin analogs)

IT 4530-20-5D, resin-bound
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide synthesis with)

IT 50-56-6DP, sarcosine-or N-methylalanine-containing analogs 107-97-1DP, oxytocin and vasopressin analogs containing 3913-67-5DP, oxytocin and vasopressin analogs containing 11000-17-2DP, sarcosine-or N-methylalanine-containing analogs 77225-24-2P 84558-69-0P **84558-73-6P 84558-74-7P** 84558-77-0P 84558-78-1P **84558-81-6P 84558-82-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of)

IT 84558-67-8P 84558-68-9P 84558-71-4P 84558-72-5P 84558-76-9P 84558-79-2P 84558-80-5P 84582-76-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking-oxidative cyclization of)

IT 84558-66-7DP, resin-bound 84558-70-3DP, resin-bound 84558-75-8DP, resin-bound 84582-77-4DP, resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation and partial deblocking-peptide coupling reaction of)

IT 84558-86-1DP, resin-bound 84558-87-2DP, resin-bound 84558-88-3DP, resin-bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and resin cleavage of, by ammonolysis)

IT 84558-83-8DP, resin-bound 84558-84-9DP, resin-bound 84558-85-0DP, resin-bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and resin-cleavage of, by ammonolysis)

IT 50903-88-3DP, resin-bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

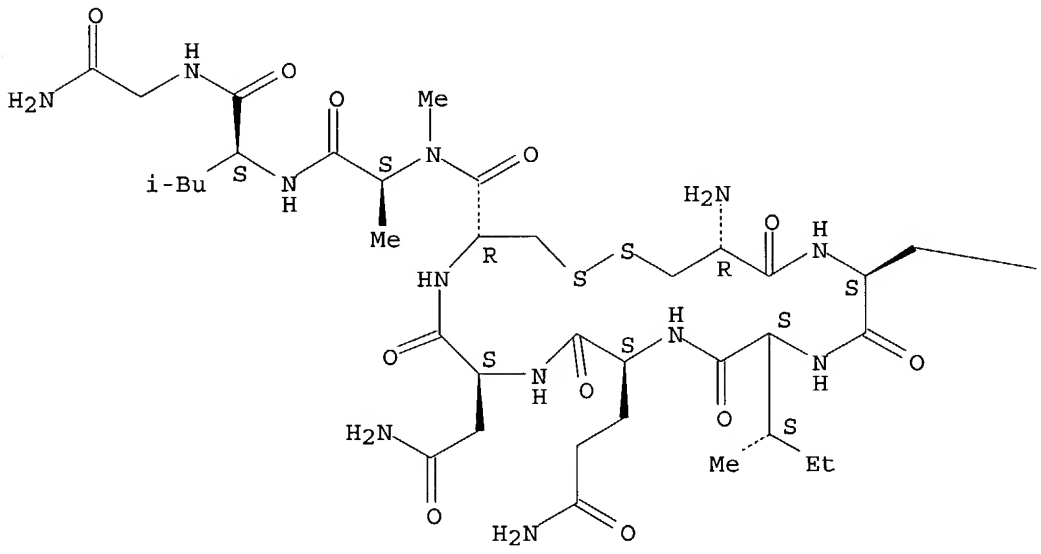
IT 2899-66-3 3257-18-9 4587-33-1 15387-45-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase peptide coupling of)

IT **84558-73-6P 84558-74-7P 84558-81-6P 84558-82-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of)

RN 84558-73-6 HCAPLUS
CN Oxytocin, 7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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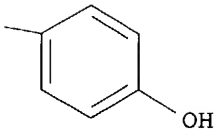
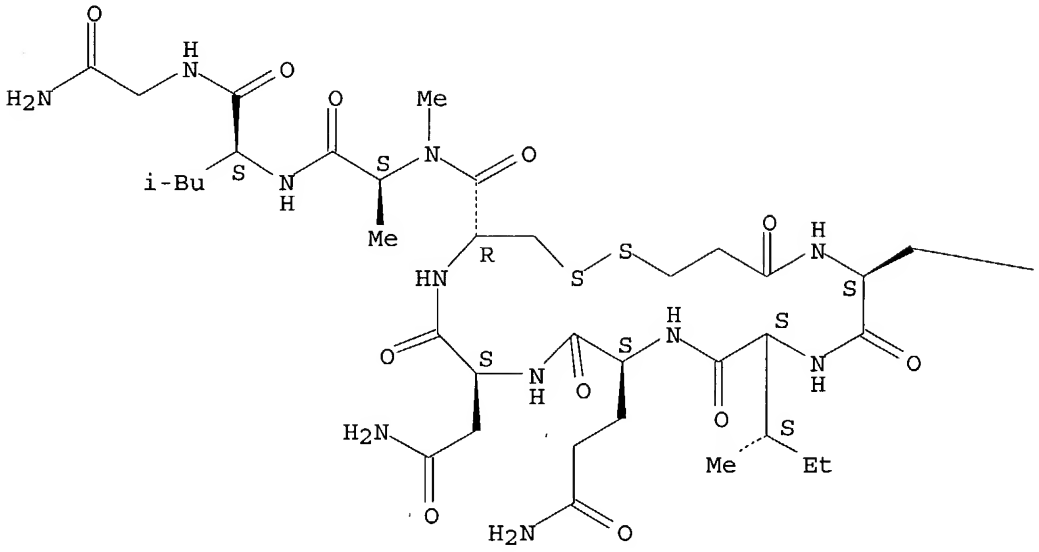


RN 84558-74-7 HCAPLUS
CN Oxytocin, 1-(3-mercaptopropanoic acid)-7-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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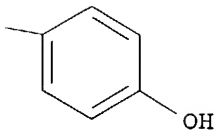
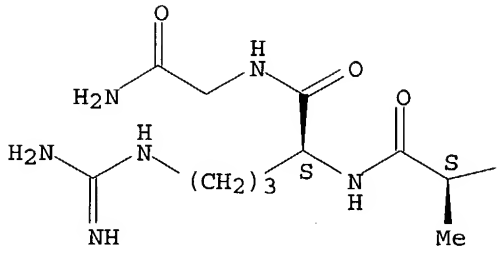


RN 84558-81-6 HCAPLUS
CN Vasopressin, 7-(N-methyl-L-alanine)-8-L-arginine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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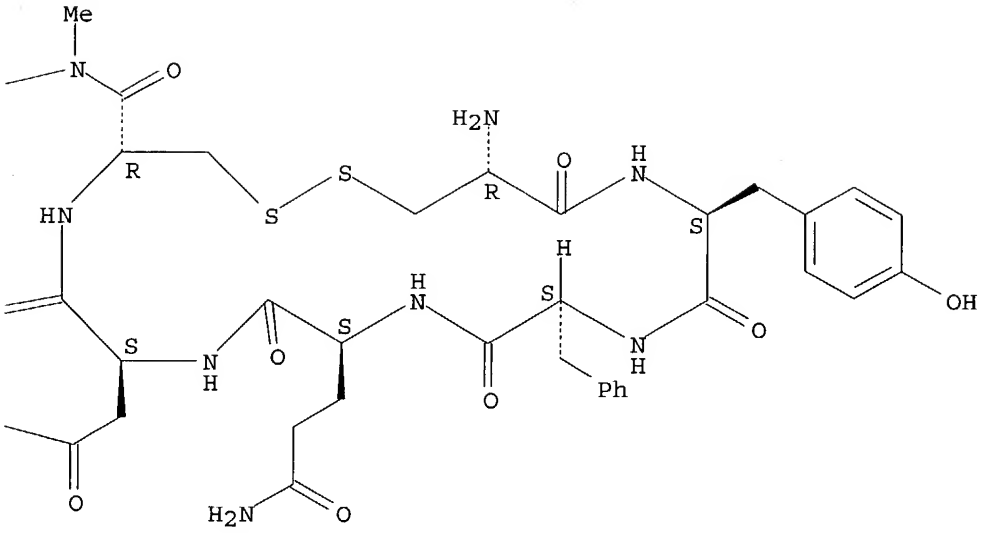
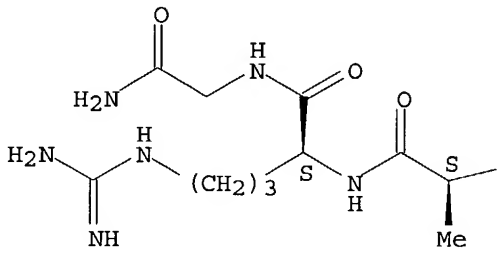


RN 84558-82-7 HCAPLUS
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-N-methyl-L-alanyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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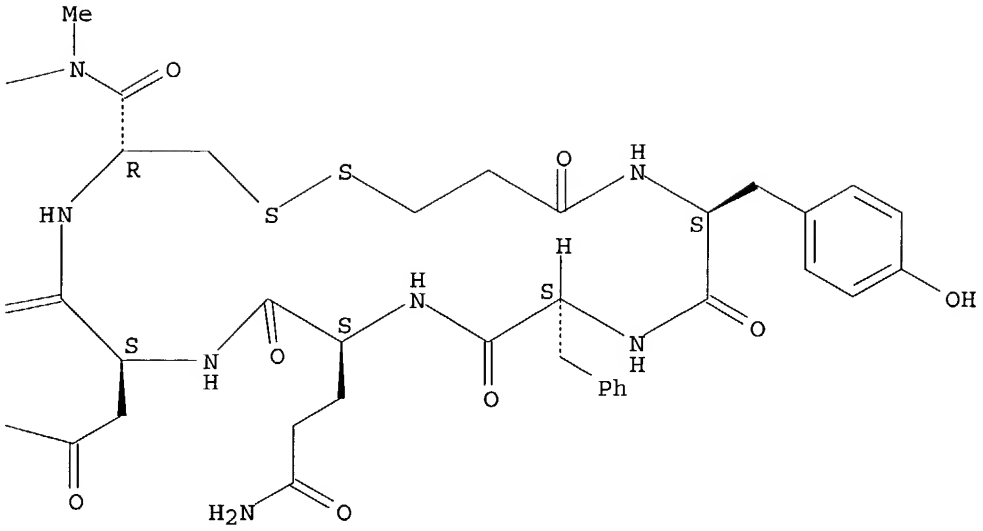

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L59 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:203814 HCAPLUS
DN 140:253449
ED Entered STN: 14 Mar 2004
TI Preparation of heterocyclylcarboxamides as oxytocin inhibitors
IN **Armour, Duncan Robert; Bell, Andrew Simon; Edwards, Paul John; Ellis, David; Hepworth, David; Lewis, Mark Llewellyn; Smith, Christopher Ronald**
PA **Pfizer** Limited, UK; **Pfizer** Inc.
SO PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D213-82
ICS C07D319-18; C07D213-81; C07D405-12; C07D521-00; C07D401-12; C07C255-57; A61K031-44; A61K031-4427; A61P015-04; A61P015-10
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 28, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004020414	A1	20040311	WO 2003-IB3705	20030813

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2002-19961 A 20020828

OS MARPAT 140:253449

AB R1CON[(CH2)xR2]C(R4)[(CH2)yR3](CH2)zR5 [R1 = (substituted) Ph, heteroaryl; R2 = (substituted) Ph, OPh, cycloalkyl, heteroaryl, heterocyclyl, etc.; R3 = (substituted) (fused) Ph, heterocyclyl, heteroaryl, R6, etc.; R4 = H, Me; R5 = CONH2, NH2, OH, R6, NHR6, OR6, CONHR6, (substituted) heteroaryl, etc.; R6 = alkyl; x, y, z = 0-2], were prepared Thus, 4-chlorobenzylamine, o-tolualdehyde, 2-aminonicotinic acid, and (4-isocyanocyclohex-3-enyl)benzene (preparation given) were stirred in MeOH/cyclohexane to give a residue which was stirred in aqueous HCl/THF to give 2-amino-N-[2-amino-1-(2-methylphenyl)-2-oxoethyl]-N-(4-chlorobenzyl)nicotinamide. Title compds. at 10 .mu.M gave >70% inhibition of oxytocin.

ST heterocyclylcarboxamide prepn oxytocin inhibitor; neuropsychiatric obsessive compulsive disorder treatment heterocyclylcarboxamide prepn; ocular arterial nephrotic hypertension treatment heterocyclylcarboxamide prepn; liver cirrhosis congestive heart failure treatment heterocyclylcarboxamide prepn; dysmenorrhea premature birth benign prostatic hypertrophy treatment heterocyclylcarboxamide prepn; obesity feeding eating appetite disorder treatment heterocyclylcarboxamide prepn; labor complication preterm labor premature ejaculation treatment heterocyclylcarboxamide prepn; sexual dysfunction treatment heterocyclylcarboxamide prepn

IT Addition reaction
(Ugi; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT Prostate gland, disease
(benign hyperplasia, treatment; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT Parturition
(complications, treatment; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT Appetite
Sexual behavior
(disorder, treatment; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT Heart, disease
(failure, treatment; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT Hypertension
(nephrotic hypertension treatment; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT Mental disorder
(obsession-compulsion, treatment; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT Sexual behavior
(premature ejaculation, treatment; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT Parturition
(premature, treatment; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT Antihypertensives
Antiobesity agents
Drug delivery systems
Human
(preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT Cirrhosis
Dysmenorrhea
Glaucoma (disease)

Hypertension
Mental disorder
Obesity
(treatment; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT **669084-63-3P**, 2-Amino-N-[2-amino-1-(2-methylphenyl)-2-oxoethyl]-N-(4-chlorobenzyl)nicotinamide **669084-64-4P**, N-[2-Amino-1-(3-methoxyphenyl)-2-oxoethyl]-4-cyano-N-(4-methylbenzyl)benzamide **669084-65-5P**, N-[3-Amino-1-(3-methoxyphenyl)-3-oxopropyl]-4-methyl-N-(4-methylbenzyl)nicotinamide **669084-66-6P**, 2-Amino-N-[(1S)-3-amino-3-oxo-1-phenylpropyl]-N-(4-methylbenzyl)nicotinamide **669084-67-7P**, 5-Chloro-2-methylthio-N-[2-amino-1-[1,4-benzodioxan-6-yl]-2-oxoethyl]-N-(4-methylbenzyl)pyrimidine-4-carboxamide **669084-68-8P**, 5-Chloro-2-amino-N-[2-amino-1-[1,4-benzodioxan-6-yl]-2-oxoethyl]-N-(4-methylbenzyl)pyrimidine-4-carboxamide **669084-69-9P**, 2-Amino-N-[carbamoyl-(2,3-dihydro-benzo[1,4]dioxin-6-yl)methyl]-4,6-dimethyl-N-(4-methylbenzyl)nicotinamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT 50-56-6, Oxytocin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT **669084-70-2P 669084-72-4P 669084-74-6P**
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669087-08-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT 669087-09-6P 669087-10-9P 669087-11-0P
669087-12-1P 669087-13-2P 669087-14-3P
669087-15-4P 669087-16-5P 669087-17-6P
669087-18-7P 669087-19-8P 669087-20-1P
669087-21-2P 669087-22-3P 669087-23-4P
669087-24-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT 74-89-5, Methylamine, reactions 75-04-7, Ethylamine, reactions
100-46-9, Benzylamine, reactions 104-84-7, 4-Methylbenzylamine
104-86-9, 4-Chlorobenzylamine 104-87-0, p-Tolualdehyde 123-00-2,

3-(4-Morpholinyl)-1-propylamine 124-40-3, Dimethylamine, reactions 529-20-4, o-Tolualdehyde 557-66-4, Ethylamine hydrochloride 591-31-1, m-Anisaldehyde 593-51-1, Methylamine hydrochloride 619-65-8, 4-Cyanobenzoic acid 934-60-1, 6-Methylpyridine-2-carboxylic acid 2260-00-6 2942-59-8, 2-Chloronicotinic acid 3222-50-2, 4-Methylnicotinic acid 3952-66-7, Methyl 2-ketobutyrate 4637-24-5, Dmf dimethyl acetal 5345-47-1, 2-Aminonicotinic acid 25016-11-9, 1-Methyl-1H-pyrazole-4-carboxaldehyde 29668-44-8, Benzodioxane-6-carboxaldehyde 41110-28-5, 3-Methylpyrazine-2-carboxylic acid 61727-33-1, 5-Chloro-2-(methylsulfanyl)pyrimidine-4-carboxylic acid 68208-19-5 69950-65-8 79686-03-6, Methyl 5-chloro-2-methylthiopyrimidine-4-carboxylate 101395-71-5, 2-(1H-Pyrazol-1-yl)ethylamine 103365-47-5 106837-89-2, 2-Amino-4,6-dimethylnicotinic acid 120351-90-8, 2-(2-Fluorophenoxy)ethylamine 128798-29-8 155790-12-8, 6-Methyl-2-methylaminonicotinic acid 158063-66-2, 4-Trifluoromethylnicotinic acid 179897-89-3, 5-Bromo-2-fluorobenzonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclylcarboxamides as oxytocin inhibitors)

IT 32399-13-6P, 2-Methylaminonicotinic acid 33522-80-4P, 2-Benzylaminonicotinic acid 67751-16-0P 128798-39-0P 218301-22-5P, 2-Fluoro-5-formylbenzonitrile 669087-25-6P, 2-Ethylaminonicotinic acid 669087-26-7P 669087-27-8P, Methyl 3-amino-3-(3-methoxyphenyl)propanoate 669087-28-9P 669087-29-0P 669087-30-3P 669087-31-4P 669087-32-5P 669087-33-6P 669087-34-7P 669087-35-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclylcarboxamides as oxytocin inhibitors)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Adipogenix Inc; WO 03007888 A 2003 HCAPLUS
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(8) Francis, G; WO 03037274 A 2003 HCAPLUS
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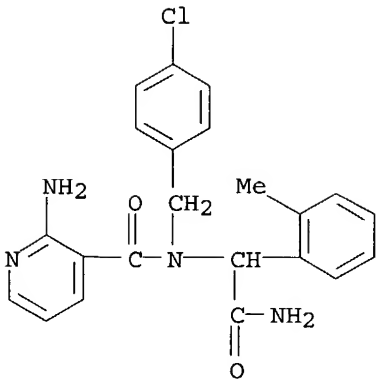
(12) Sasaki, Y; CHEMICAL & PHARMACEUTICAL BULLETIN 1993, V41(3), P415 HCAPLUS
(13) Tokuyama Soda Kk; EP 0189774 A 1986 HCAPLUS
(14) Tomita, K; US 4060402 A 1977 HCAPLUS
(15) Wyeth; WO 0244142 A 2002 HCAPLUS

IT **669084-63-3P**, 2-Amino-N-[2-amino-1-(2-methylphenyl)-2-oxoethyl]-N-(4-chlorobenzyl)nicotinamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of heterocyclylcarboxamides as oxytocin inhibitors)

RN 669084-63-3 HCAPLUS

CN 3-Pyridinecarboxamide, 2-amino-N-[2-amino-1-(2-methylphenyl)-2-oxoethyl]-N-[(4-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)



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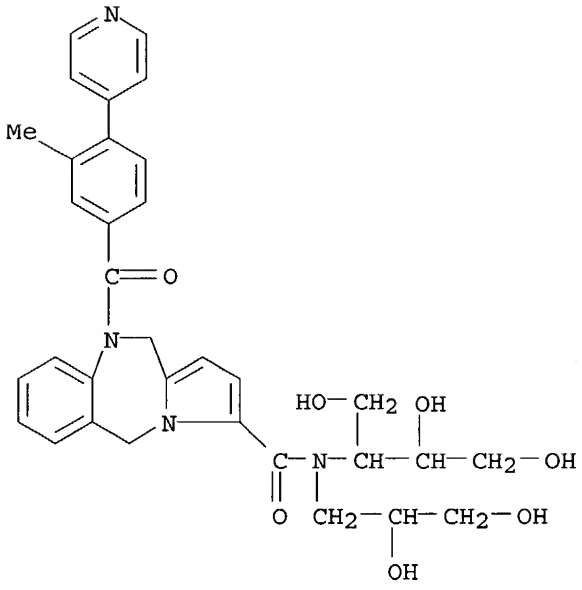
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr l61 tot

L61 ANSWER 1 OF 3 USPATFULL on STN
AN 2003:24183 USPATFULL
TI Novel tricyclic hydroxy carboxamides and derivatives thereof tocolytic oxytocin receptor antagonists
IN Arturo Failli, Amedeo, Princeton Junction, NJ, UNITED STATES
Shumsky, Jay Scott, Hightstown, NJ, UNITED STATES
Caggiano, Thomas Joseph, Morrisville, PA, UNITED STATES
Sabatucci, Joseph Peter, Collegeville, PA, UNITED STATES
Memoli, Kevin Anthony, Cranbury, NJ, UNITED STATES
Trybulski, Eugene John, Princeton Junction, NJ, UNITED STATES
Sanders, William Jennings, Fox Lake, IL, UNITED STATES
PA Wyeth, Madison, NJ, UNITED STATES (U.S. corporation)
PI US 2003018026 A1 20030123
AI US 2002-120100 A1 20020410 (10)
PRAI US 2001-283261P 20010412 (60)
DT Utility
FS APPLICATION
LREP Arnold S. Milowsky, 5 Giralda Farms, Madison, NJ, 07940
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4624
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides novel substituted tricyclic carboxamides which act as oxytocin receptor competitive antagonists, as well as methods of their manufacture, pharmaceutical compositions and methods of their use in treatment, inhibition, suppression or prevention of preterm labor, dysmenorrhea and endometritis, suppression of labor at term prior to caesarean delivery, and to facilitate antinatal transport to a medical facility. These compounds are also useful in enhancing fertility rates, enhancing survival rates and synchronizing estrus in farm animals; and may be useful in the prevention and treatment of disfunctions of the oxytocin system in the central nervous system including obsessive

compulsive disorder (OCD) and neuropsychiatric disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **473610-58-1P**
(preparation of novel tricyclic benzodiazepine carboxamides as tocolytic oxytocin receptor antagonists)
RN 473610-58-1 USPATFULL
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide, N-[2,3-dihydroxy-1-(hydroxymethyl)propyl]-N-(2,3-dihydroxypropyl)-10,11-dihydro-10-[3-methyl-4-(4-pyridinyl)benzoyl]- (9CI) (CA INDEX NAME)

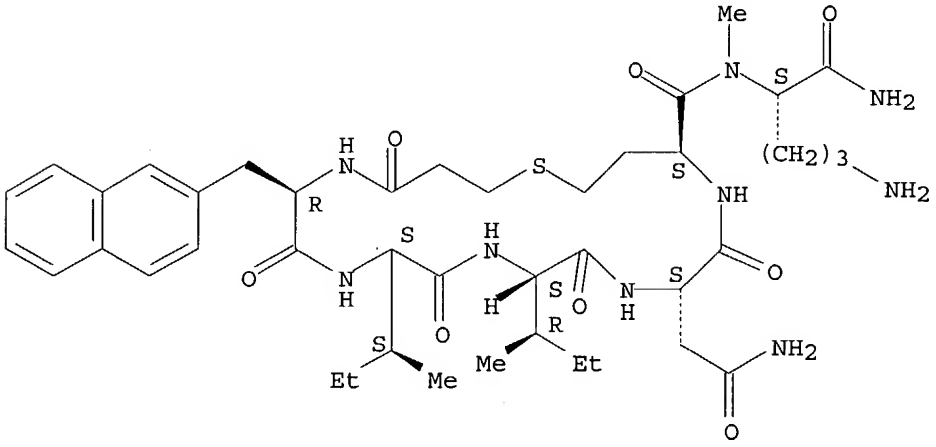


L61 ANSWER 2 OF 3 USPATFULL on STN
AN 2000:150142 USPATFULL
TI Heptapeptide oxytocin analogues
IN Melin, Per, Malmo, Sweden
Nilsson, Anders, Lund, Sweden
Trojnar, Jerzy, Solana Beach, CA, United States
Aurell, Carl-Johan, Molndal, Sweden
Riviere, Pierre, San Diego, CA, United States
Haigh, Robert, Hants, United Kingdom
PA Ferring, B.V., Hoofddorp, Netherlands (non-U.S. corporation)
PI US 6143722 20001107
WO 9823636 19980604
AI US 1999-308912 19990802 (9)
WO 1997-SE1968 19971121
19990802 PCT 371 date
19990802 PCT 102(e) date
PRAI SE 1996-4341 19961126
DT Utility
FS Granted
EXNAM Primary Examiner: Davenport, Avis M.
LREP Hopgood, Calimafde Kalil & Judlowe
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 693
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Heptapeptide analogues or pharmaceutically acceptable salts thereof consist of a hexapeptide moiety S and a C-terminal .beta.-aminoalcohol residue Z bound to the moiety S by an amide bond, wherein the .beta.-aminoalcohol Z is --NR--CH(Q)--CH.sub.2 OH, Q is (CH.sub.2).sub.n --NH--A is H or --C(.dbd.NH)NH.sub.2, and R is CH.sub.3 or C.sub.2 H.sub.5, and the moiety S wherein H is a D-aromatic .alpha.-aminoacid and Y is an aliphatic .alpha.-aminoacid and have oxytocin antagonist activity. Also disclosed is: a method of their synthesis; pharmaceutical compositions containing these analogues; the synthesis of such compositions; a method of control of uterine contractions.

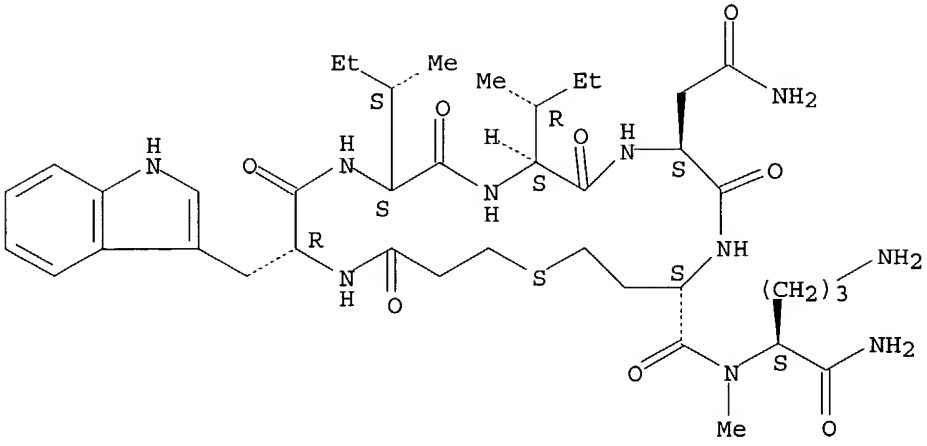
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **163618-99-3P 176742-08-8P 208400-60-6P**
208400-61-7P 208400-62-8P 208400-63-9P
208400-64-0P 208400-65-1P 208400-66-2P
208400-67-3P 208400-68-4P 208400-69-5P
208400-71-9P 208400-73-1P 285571-64-4P
(preparation of heptapeptide alc. oxytocin analogs)
RN 163618-99-3 USPATFULL
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



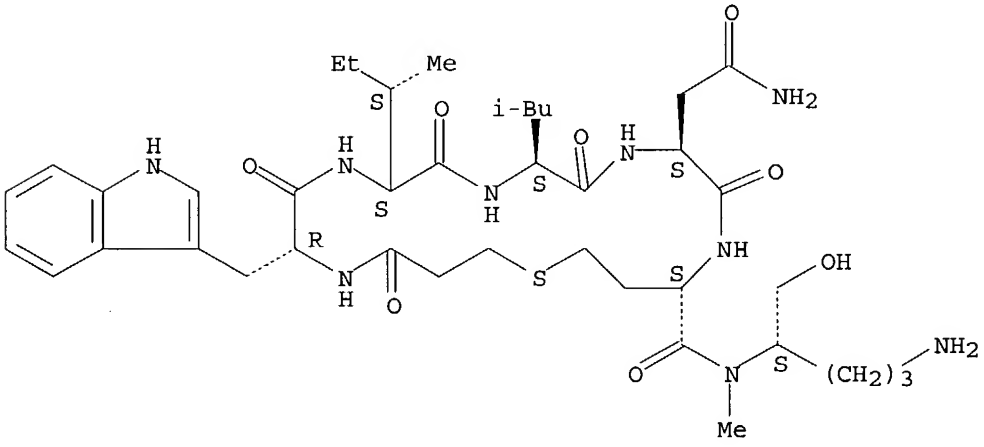
RN 176742-08-8 USPATFULL
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



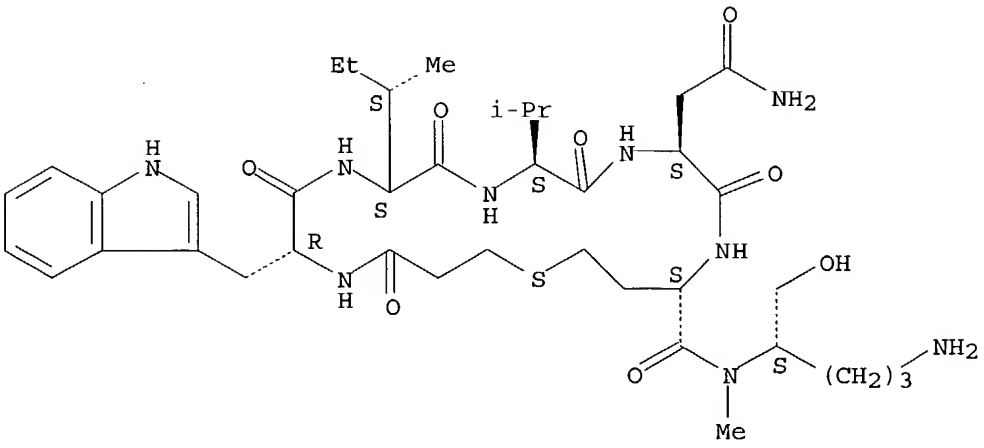
RN 208400-60-6 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-leucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



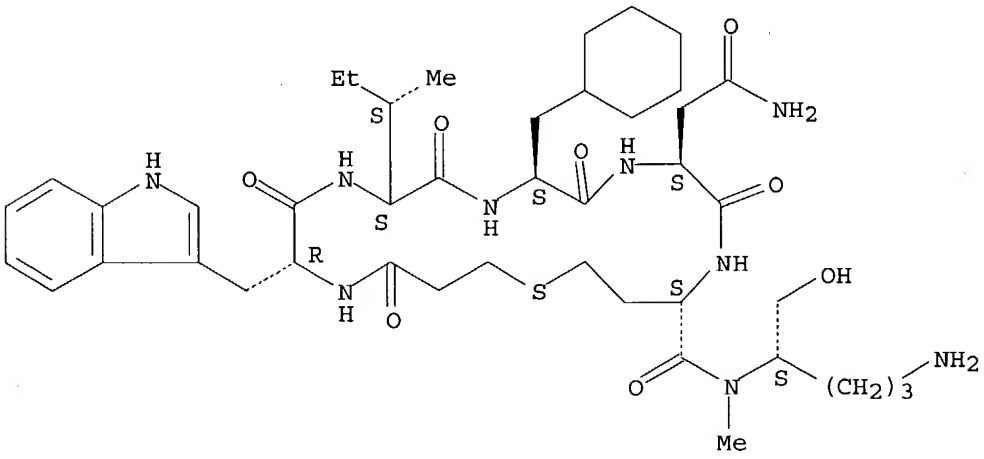
RN 208400-61-7 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-valyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



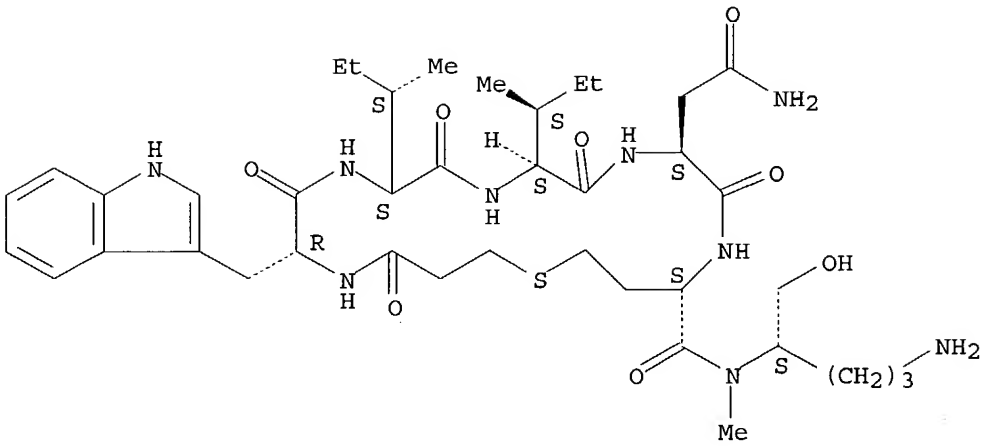
RN 208400-62-8 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-3-cyclohexyl-L-alanyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



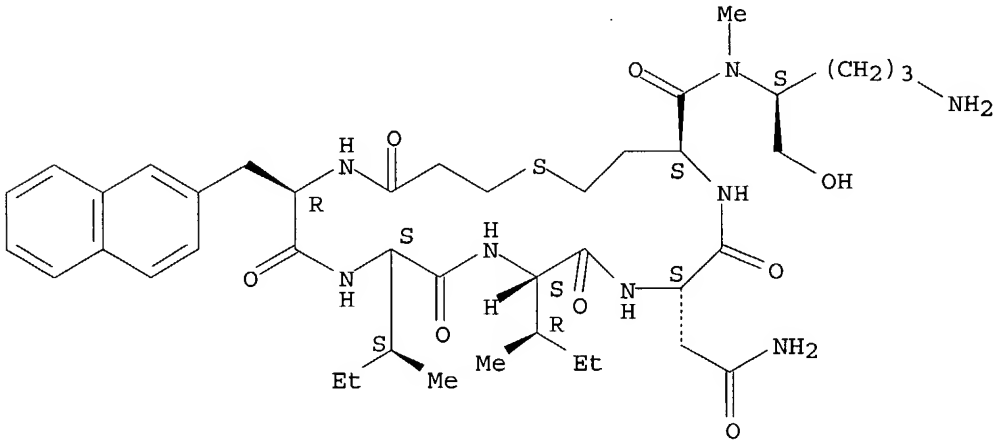
RN 208400-63-9 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-isoleucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



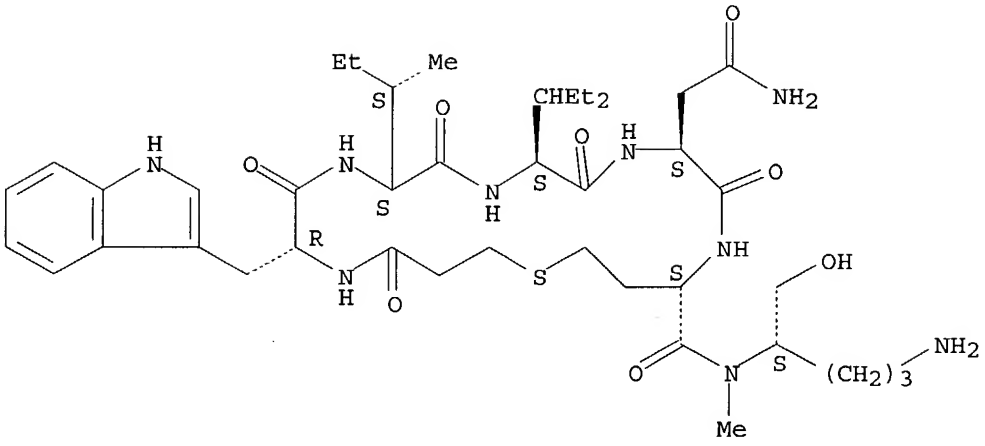
RN 208400-64-0 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



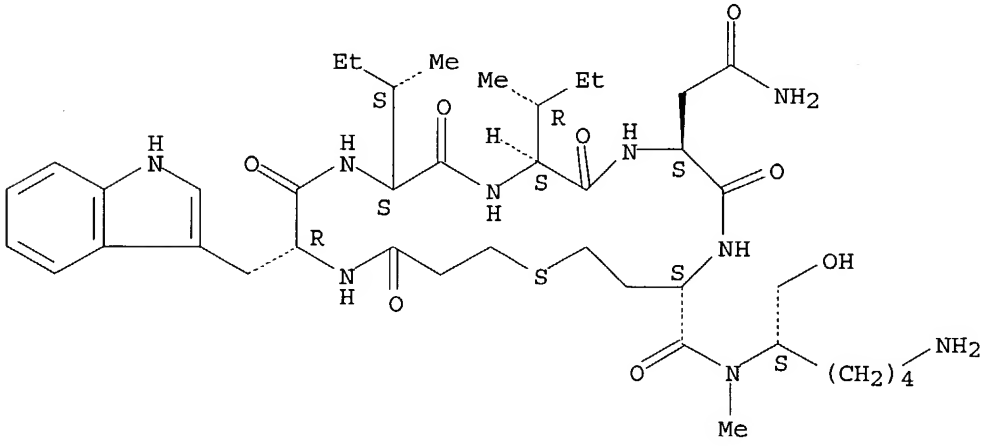
RN 208400-65-1 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-3-ethyl-L-norvalyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



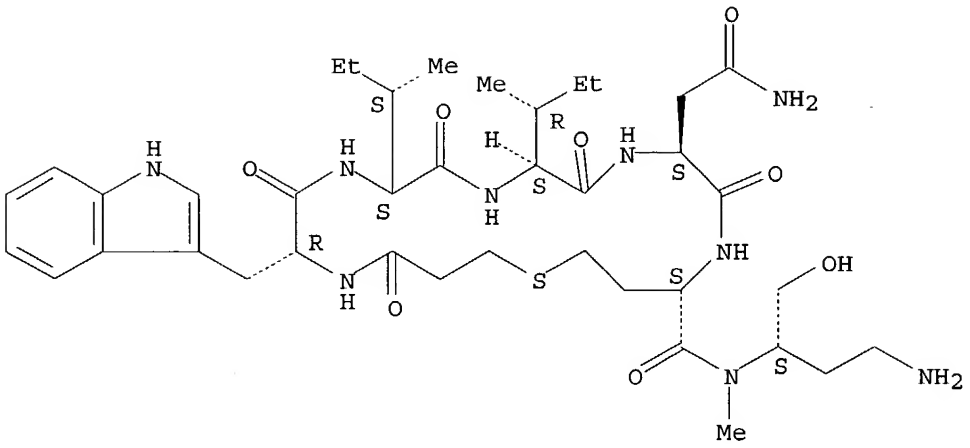
RN 208400-66-2 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-5-amino-1-(hydroxymethyl)pentyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 208400-67-3 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-3-amino-1-(hydroxymethyl)propyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

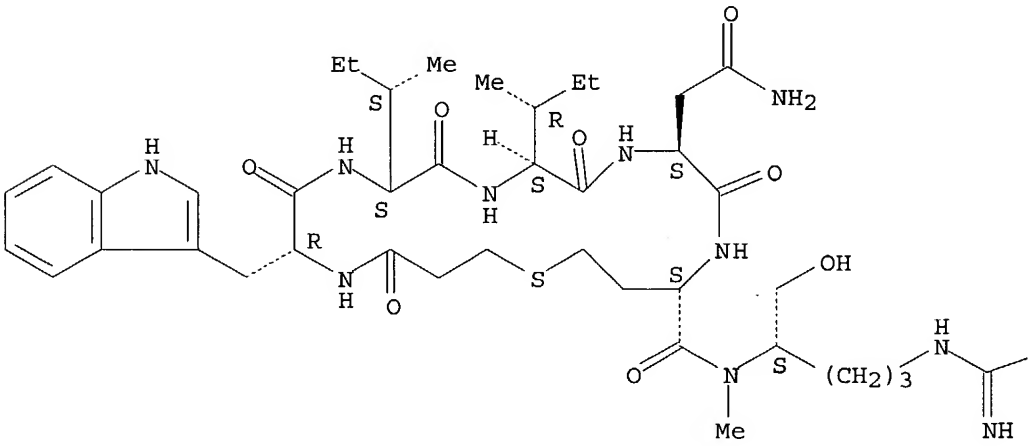
Absolute stereochemistry.



RN 208400-68-4 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-4-[(aminoiminomethyl)amino]-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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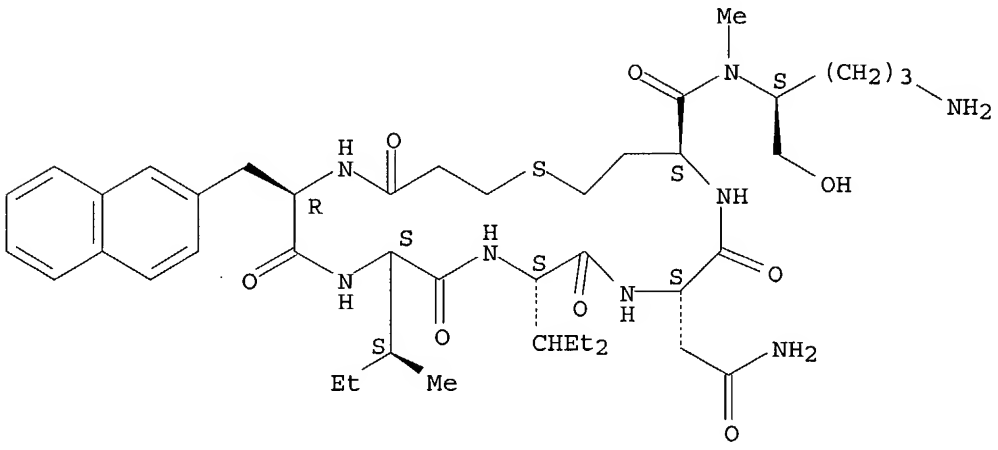
NH_2

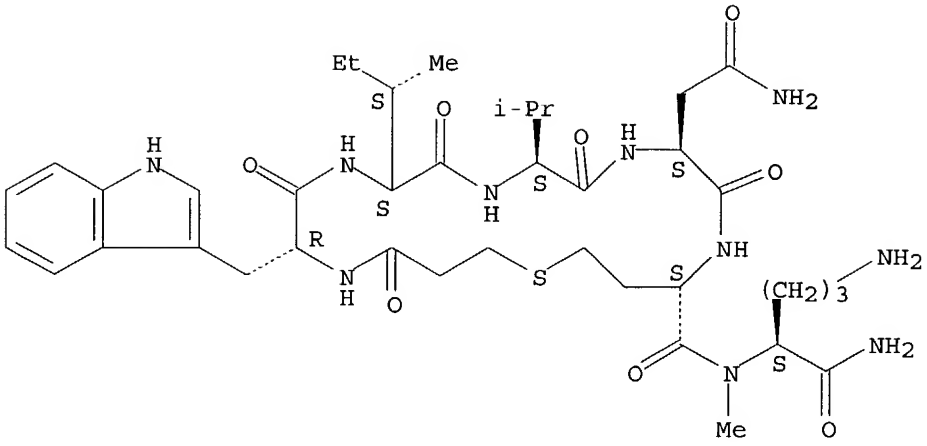
RN 208400-69-5 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-3-(2-naphthalenyl)-D-alanyl-L-isoleucyl-3-ethyl-L-norvalyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



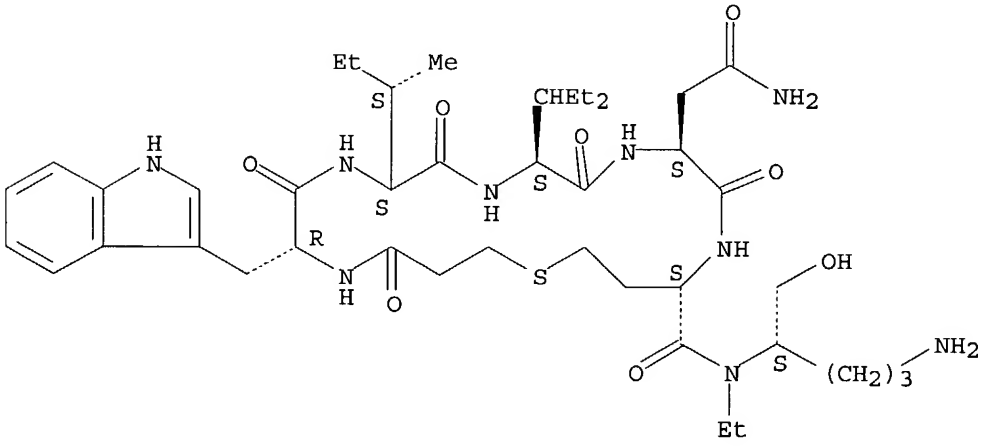
RN 208400-71-9 USPATFULL
CN L-Ornithinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-valyl-L-asparaginyl-L-homocysteinyl-N2-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



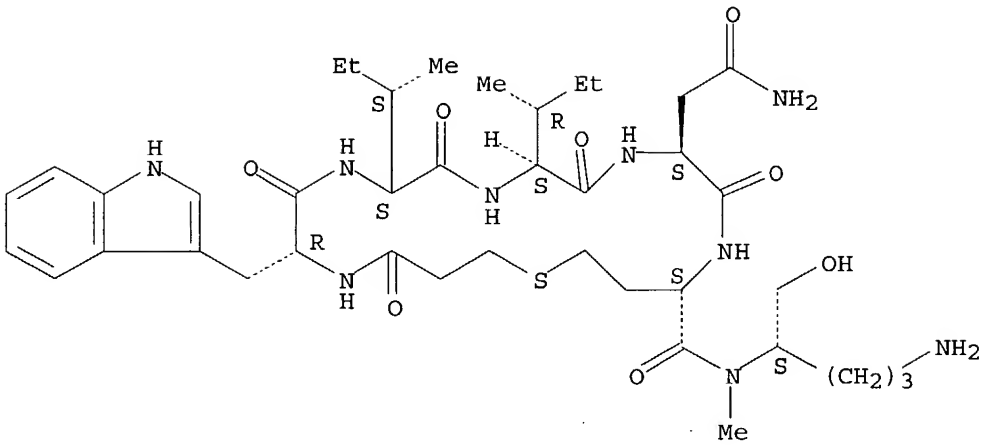
RN 208400-73-1 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-3-ethyl-L-norvalyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-ethyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 285571-64-4 USPATFULL
CN L-Homocysteinamide, N-(3-mercapto-1-oxopropyl)-D-tryptophyl-L-isoleucyl-L-alloisoleucyl-L-asparaginyl-N-[(1S)-4-amino-1-(hydroxymethyl)butyl]-N-methyl-, cyclic (1.fwdarw.5)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.

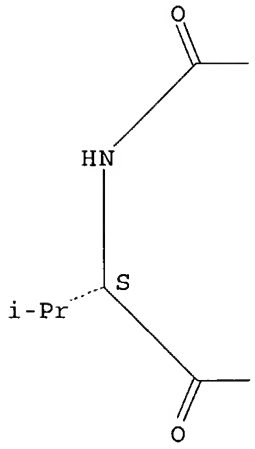


L61 ANSWER 3 OF 3 USPATFULL on STN
AN 88:1269 USPATFULL
TI ARG.sup.7 -ARG.sup.8 -vasopressin antagonists
IN Ali, Fadia E., Cherry Hill, NJ, United States
PA SmithKline Beckman Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 4717715 19880105
AI US 1986-877571 19860623 (6)
DT Utility
FS Granted
EXNAM Primary Examiner: Phillips, Delbert R.
LREP Williams, Janice E., Suter, Stuart R., Lourie, Alan D.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 738
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Vasopressin antagonists which have a dipeptide side chain comprised of two basic amino acids demonstrate potent V.sub.1 and V.sub.2 -antagonist activity. A species of the invention, which is prepared by conventional peptide sequencing, is [1-(.beta.-mercapto-.beta.,.beta.-cyclopentamethylene propionic acid)-2-(O-ethyl)-D-tyrosine-4-valine-7-arginine-8-arginine-9-desglycine]-vasopressin.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **110500-82-8P**
(preparation of, as vasopressin antagonist and diuretic)
RN 110500-82-8 USPATFULL
CN L-Argininamide, O-ethyl-N-[(1-mercaptocyclohexyl)acetyl]-D-tyrosyl-L-phenylalanyl-L-valyl-L-asparaginyl-L-cysteinyl-N2-methyl-L-arginyl-, cyclic (1.fwdarw.5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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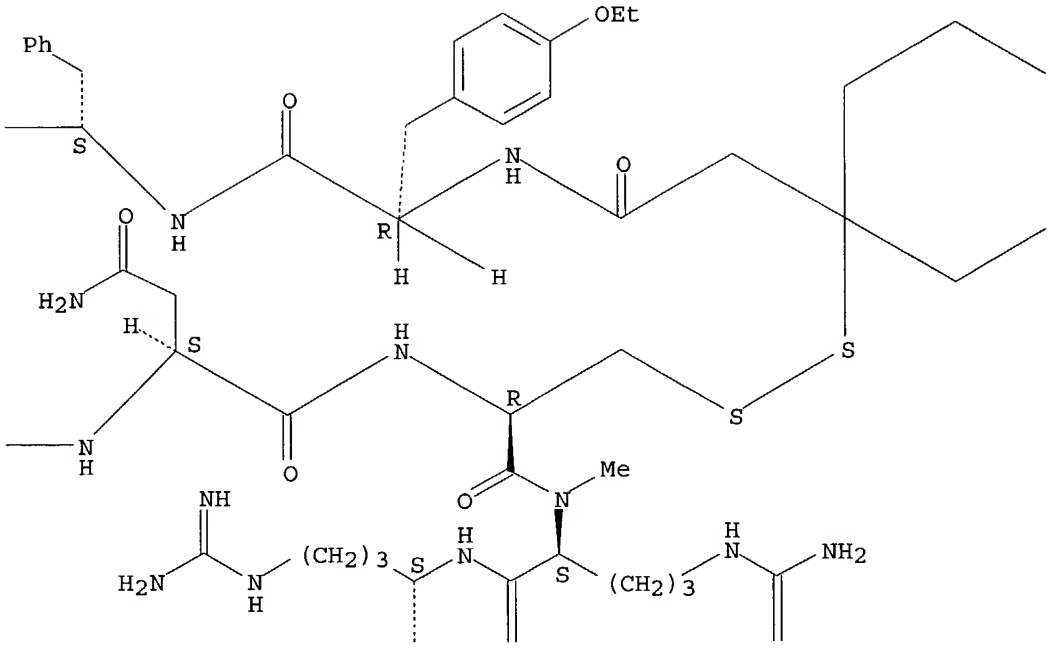

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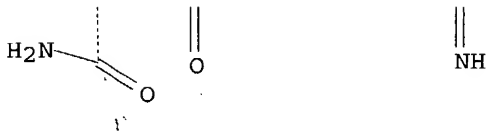
PAGE 2-B



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